IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF WEST VIRGINIA
Clarksburg

ACTELION PHARMACEUTICALS LTD.,

Plaintiff,

v.

CIVIL ACTION NO. 1:20-CV-110
Judge Bailey

MYLAN PHARMACEUTICALS, INC.,

Defendant.

SEALED ORDER

On February 20, 2024, the Court held a one-day trial to determine whether Mylan Pharmaceuticals Inc.'s ANDA product infringed the limitation "pH of 13 or higher" as used in the Asserted Claims of U.S. Patent Nos. 8,318,802 ("the '802 patent") and 8,598,227 ("the '227 patent").

Below are this Court's Findings of Fact and Conclusions of Law:

I. FINDINGS OF FACT

A. Summary

1. This is a patent infringement action brought by Actelion under the provisions of the Hatch-Waxman Act, 21 U.S.C. § 355(j) alleging infringement of claims 1, 6, 8, 10–11, 16, 18, 20, and 22 of U.S. Patent No. 8,318,802 ("the '802 patent") and claims 16, 18–22, and 24–42 of U.S. Patent No. 8,598,227 ("the '227 patent") (collectively, "the Asserted Claims" and "the patents-in-suit").

2. The only dispute at trial was whether the pH of the bulk solution used to form Mylan's ANDA product is "13 or higher." [Doc. 221 at ¶ 70]. That sole dispute implicates the "plain and ordinary meaning" of the term "pH of 13," which in turn implicates the proper construction of the term "pH"—is pH as claimed measured at standard temperature or at an unspecified temperature dependent on the manufacturing conditions of an accused product? [Doc. 225 at 3:8–21]; [Doc. 221 at ¶¶ 70–72].

3. The facts of the case are: (i) a POSA reading the intrinsic evidence would understand the claimed "pH" value of "13 or higher" (*i.e.*, 12.98 or higher) to have its plain and ordinary meaning of being taken at standard temperature, which is consistent with the well-known industry standard (*i.e.*, the USP); (ii) the references initially put forward by Actelion, and other extrinsic evidence, also confirm the plain and ordinary meaning of "pH"; (iii) Mylan's ANDA product will not be formed from a bulk solution having a pH of 13 (12.98) or higher; (iv) Actelion did not, and cannot, meet its burden to establish infringement, either literally or under the doctrine of equivalents; (v) accepting Actelion's position would render the Asserted Claims indefinite.

B. The Parties

4. Actelion holds approved New Drug Application ("NDA") No. 022260, under which the United States Food and Drug Administration ("FDA") granted approval for epoprostenol sodium for injection, 0.5 mg/vial and 1.5 mg/vial, both marketed under the trade name VELETRI®. [Doc. 1 at ¶ 14].

5. Actelion is the assignee of the '802 and '227 patents. [Doc. 219-2 at ¶ 127].

6. Actelion's VELETRI® product practices the asserted claims. [Id. at ¶ 128].

7. Mylan Pharmaceuticals, Inc. ("Mylan") filed Abbreviated New Drug Application ("ANDA") No. 213913, seeking FDA approval to market a generic version of VELETRI®. PTX-64.0001.

C. Live Witnesses

i. Christian Schöneich, Ph.D.

8. Actelion presented the testimony of Dr. Christian Schöneich, Ph.D., who was recognized by the Court as an "expert in pharmaceutical chemistry, including formulation instability." [Doc. 225 at 14:13–15].

9. Dr. Schöneich admitted that prior to this case, the last time he conducted a pH measurement at a low temperature was in the 1980s, before obtaining his Ph.D. [Doc. 225 at 45:8–13 (Schöneich cross)]; [Doc. 225 at 11:23 (Schöneich) (obtained Ph.D. in Germany in 1990)]. At the time of his deposition, he could not recall ever publishing a scientific article where pH measurements were made and reported at a low temperature. [Doc. 225 at 46:11–15 (Schöneich cross)].

10. Dr. Schöneich did not address the specification of the patents-in-suit, including the Examples, during Actelion's case-in-chief. [Doc. 225 at 75:8–13 (Schöneich cross) ("Q. And I know you had indicated too that you had reviewed the specification, but I couldn't help but notice, on your direct, you didn't give any testimony on your -- on the examples or the specification in connection with your opinions, correct? A. That's correct."]. Dr. Schöneich's position that the "bulk solution having a pH of 13 or higher" refers to "operating temperature" is unsupported by the intrinsic record. Nowhere does the intrinsic record discuss, let alone define, the bulk solution's "actual" or "operating" temperature.

11. Nor did Dr. Schöneich provide a clear, applicable definition of "operating temperature," instead using it in contexts that appeared to refer to different things—even though his opinion rested entirely on that concept. [Doc. 225 at 29:18–30:1, 38:5–7, 53:14–19, 54:1–4, 54:21–25 (Schöneich)].

ii. William Hensler, Ph.D.

12. Mylan presented the expert testimony of Dr. William Hensler who was recognized by the Court as "an expert in the field of pharmaceuticals, including the operations used to produce bulk solutions of pharmaceuticals and the measurement of pH of those solutions." [Doc. 225 at 121:6–9].

13. Dr. Hensler testified that Mylan's proposed generic epoprostenol products do not, and will not, infringe any Asserted Claim, either literally or under the doctrine of equivalents. [Doc. 225 at 121:13–122:1, 143:24–144:6 (Hensler) ("Mylan follows USP standards for measuring their pH in producing this product. And that standard is the pH is measured at 25 degrees according to that USP standard. And Mylan clearly states that in their ANDA [redacted] And that does not infringe on the value of 12.98.")]; [Doc. 225 at 144:12–146:5 (Hensler) (testimony regarding disclosure dedication)]; [Doc. 225 at 146:6–148:1 (Hensler) (testimony regarding prosecution history estoppel, including whether the amendment bore a tangential relation to the alleged equivalent)]; [Doc. 225 at 148:3–11 (Hensler) (testifying that the alleged equivalent (12.5–12.8) was foreseeable at the time of the amendment)].

14. Dr. Hensler testified regarding a POSAs knowledge and understanding of the art in the context of pharmaceutical manufacturing as it relates to the plain and ordinary meaning of "pH". *See, e.g.*, [Doc. 225 at 122:15–128:21 (Hensler)].

D. Technological Background

i. Standard Ambient Temperature and Pressure and pH

15. 25 ± 2°C is known as "standard temperature" and is a component of "standard ambient, temperature, and pressure" ("SATP"), an industry benchmark for standardizing measurements. [Doc. 225 at 123:18–21 (Hensler)]; [Doc. 225 at 42:19–21 (Schöneich) ("Q. When you use the term 'standard temperature for measuring pH,' you mean 25 degrees, correct? A. Yes.")]; DTX-67.013–14 (Silberberg); DTX-66.019 (Kessel); DTX-65.024 (Mustoe).

16. The pH scale was discovered over a century ago and was developed "as a way to express in a convenient way the acidity or the alkalinity of a solution." [Doc. 225 at 123:4–5 (Hensler)]; DTX-67.013 (Silberberg); ***Dow Chem. Co. v. Halliburton Co.***, 631 F.Supp. 666, 688–89 (N.D. Miss. 1985), *aff'd sub nom.* ***Halliburton Co. & Mississippi Power & Light Co. v. Dow Chem. Co.***, 790 F.2d 93 (Fed. Cir. 1986).

17. The ordinary meaning of "neutral" pH is only defined as 7.0 at SATP. DTX-66.012, 019 (Kessel); DTX-67.013 (Silberberg); DTX-65.024 (Mustoe). At SATP, a basic or alkaline environment is one where pH is greater than 7.0. [Doc. 225 at 43:1–3 (Schöneich) (testifying that it is "true for 25 degrees")]. The patentee adopted this standard in defining an "alkalinizing agent" in the patents-in-suit as "an agent that provides alkaline environment (pH>7) when epoprostenol is dissolved in water along with the alkalinization agent." JTX-1.0003 (col. 4, ll. 62–64); JTX-2.0004 (col. 5, ll. 3–5); [Doc. 225 at 124:18–125:7 (Hensler)]; [Doc. 225 at 43:22–44:3 (Schöneich)]. This statement is only true if the pH is measured at standard temperature. [Doc. 225 at 125:2-3 (Hensler)];

[Doc. 225 at 43:1-3 (Schöneich)]; DTX-66.012 (Kessel). That is because it is an undisputed, scientific fact that temperature has an impact on pH—as temperature decreases, pH increases. [Doc. 225 at 7:15–16, 66:12–13 (Schöneich)]; [Doc. 225 at 124:8–10 (Hensler)]. In other words, the patents-in-suit clearly define a "neutral" pH as "7".

18. Textbooks introduced by Actelion and upon which this Court relied in its claim construction decision confirm that the pH scale and pH values when generally described *assume* SATP measurement. DTX-66.012, 019 (Kessel); DTX-67.013 (Silberberg); DTX-65.024 (Mustoe); *see* [Doc. 225 at 43:9-44:5 (Schöneich) (discussing DTX-65 (Mustoe) where the table depicts pH values and concentration equivalents as measured at standard temperature because it defines "neutral" pH as "pH of 7")]; Aug. 11, 2021, ***Markman*** Hearing [Doc. 101 at 22:14–15 ("And POSAs routinely use this pH scale just like the patentee did.")].

ii. United States Pharmacopeia

19. The United States Pharmacopeia ("USP") is a "well-recognized standard in the pharmaceutical industry [that] would be familiar to a skilled artisan." [Doc. 207 at 24]; [Doc. 225 at 126:4–5 (Hensler) ("[USP standards are] the bible for the industry. They are the gold -- the go-to standard.")].

20. The USP is used by pharmaceutical formulators and manufactures as it provides and defines, among other things, processes and standards for use in the pharmaceutical industry. [Doc. 225 at 125:17–21 (Hensler) ("Those standards, those specifications, those testing methods, those are based in the United States Pharmacopeia, which, by the way, existed before the FDA did. So everything that we do in our business

in the pharmaceutical industry comes from the USP.")]; [Doc. 225 at 49:23–50:17 (Schöneich) (discussing PTX-175 for which he relied in forming his opinions)]; PTX-175.0001 ("USP is an official quality standard for medicines marketed in the US. In addition, USP is utilized in over 140 countries worldwide and integrated into the laws of more than 40 countries"); PTX-175.0001 ("General Chapters provide broadly applicable information to industry on accepted processes, tests and methods to support product development and manufacturing for innovative, generic, and biosimilar medicines.").

21. It is undisputed that a POSA at the time of the alleged invention of the patents-in-suit would be aware of, look to, and rely upon the USP, which Actelion's expert testified was "an influential document." [Doc. 225 at 47:6-10 (Schöneich cross)];[Doc. 225 at 126:20–127:5 (Hensler) (POSAs would rely on USP in February 2006)]; [Doc. 225 at 48:24–49:5 (Schöneich cross) (POSAs would consult and rely on the USP in connection with pharmaceutical manufacturing)]. POSAs in the field of pharmaceutical manufacturing rely upon and incorporate USP standards at every stage of the development and manufacturing process. [Doc. 225 at 125:17–126:1 (Hensler)].

22. The USP standard for pH measurements applicable to pharmaceutical manufacturing is USP <791>. DTX-6.002; [Doc. 225 at 126:6–14 (Hensler) ("So this is the general section written for the -- specific to the measurement of pH. And very clearly at the bottom it states that measurements are to be made at 25 plus or minus 2 degrees unless otherwise specified in -- an individual monograph or herein.")]; [Doc. 225 at 52:2–10 (Schöneich)]. According to USP <791>, "[m]easurements are made at 25 ± 2[°C], unless otherwise specified in the individual monograph or herein." DTX-6.002; [Doc. 225 at 126:10–14 (Hensler)]; [Doc. 225 at 52:2–5 (Schöneich)]. It is undisputed that there is no

individual USP monograph concerning manufacturing criteria or measurement specifications for epoprostenol or epoprostenol solutions. [Doc. 225 at 28:18–20 (Schöneich) ("Q. Now, is epoprostenol, the substance we're talking about in this case, is that part of the compendium? A. I have not seen it in there.")]; [Doc. 225 at 171:20–22, 190:21–25 (Hensler)].

23. The only other portion of the USP (the "herein") discussing pH is related to calibration of pH meters in the event an individual monograph specifies taking pH measurements at temperatures other than 25 ± 2°C. [Doc. 225 at 127:25–128:17 (Hensler)]; DTX-6.003.

24. A POSA "would view these patents through the lens of the USP [<791>]" and would have applied those standards to the manufacture of a bulk solution. [Doc. 225 at 127:6-9, 126:6-127:1 (Hensler)]. Notably, there is no reason why a POSA would have been incapable of applying USP standards in reviewing the patents-in-suit or manufacturing epoprostenol products formed from a bulk solution. [Doc. 225 at 127:10–13 (Hensler)].

E. Actelion failed to meet its burden to establish infringement.

25. All evidence—intrinsic and extrinsic—support the conclusion that a POSA understands "pH" to carry the plain and ordinary meaning in the pharmaceutical-manufacturing industry (*i.e.*, a value measured by default at a standard temperature). A POSA would not understand pH in the patents-in-suit as an abstract concept simply describing concentration of hydrogen[1] ions at non-standardized

[1] "Hydrogen ion" is just another term for "hydronium ion." [Doc. 225 at 16:23–24 (Schöneich)].

temperatures. [Doc. 225 at 123:8–14 (Hensler)]. Dr. Hensler unambiguously testified that his interpretation of "pH" within the context of the patents was consistent with the "plain and ordinary" meaning of the term to the POSA as of the relevant priority date, [Doc. 225 at 126:20–127:9], whereas Dr. Schöneich offered no such testimony. As discussed below, the entirety of the intrinsic record (the claims, specification, and prosecution history) does not specify a temperature for pH measurement, meaning the pH values therein are measured at standard temperature. *See* [Doc. 225 at 134:21–135:14 (Hensler)].

i. The Asserted Claims

26. Each of the Asserted Claims requires that the product is "formed from a bulk solution having a pH of 13 or higher" where a "pH of 13" has been construed as "12.98" or higher. [Doc. 225 at 121:16–20 (Hensler)]; [Doc. 225 at 6:15-17 (Schöneich)]. Claim 1 of the '807 patent is exemplary of the asserted claims:

> 1. A lyophilized pharmaceutical composition comprising:
> (a) a unit dose of 0.5 mg or 1.5 mg of epoprostenol or a salt thereof;
> (b) arginine; and
> (c) sodium hydroxide,
> wherein said lyophilized pharmaceutical composition is (i) formed from a bulk solution having a pH of 13 or higher and (ii) capable of being reconstituted for intravenous administration with an intravenous fluid.

PTX-8 ('802 Patent) at cl. 1. *See also* id. at cls. 6, 8, 10, 11, 16, 18, 20, and 22; PTX-9 ('227 patent) at cls. 16, 18-22, 24–42.

27. The patent claims are directed to the pH of the bulk solution when made for an important reason. As the Patent Examiner noted, the pH of the bulk solution when made "imparts a critical function." DTX-5.039. Namely, very high pH "protect[s] against

degradation and improve[s] manufacturing stability," because degradation pathways for epoprostenol are catalyzed by hydrogen ions. [Doc. 225 at 15:23–17:7 (Schöneich)]; PTX-134. Mylan's expert acknowledged that this manufacturing stability is a key purpose of the patented invention. [Doc. 225 at 138:23–139:1 (Hensler) ("Q. Do you recall what you had noted just a few moments ago as to the purpose of the invention? A. The purpose of the invention is to show improved stability at higher pH values.")].

28. It is undisputed that the claims at issue do not specify any temperature for measurement. [Doc. 225 at 75:5–7 (Schöneich) ("Q. It doesn't specify any kind of numerical temperature, correct? A. A numerical temperature is not explicitly stated.")]; [Doc. 225 at 134:4–6 (Hensler) ("Q. Do the claims of either patent specify a temperature that the pH measurement should be made at? A. No, they don't.")]. Both experts agreed that when there is no temperature listed, a POSA understands that the pH measurements are made at standard temperature (*i.e.*, 25 ± 2?). [Doc. 225 at 28:8–10 (Schöneich) ("And if they contain pH information and no temperature statement, then these measurements are made at 25 plus/minus 2 degrees."); [Doc. 225 at 132:21–24 (Hensler) ("They didn't state a temperature at which that bulk solution has a value of 13. But again, being a POSA and reading that, I would interpret that as saying your temperature at 25 degrees.")].

29. The Asserted Claims simply require that the bulk solution have a pH of 13 or higher. This high pH can be achieved through any technique to create a solution with low hydrogen ion concentration, including cold temperature, addition of base, or both. [Doc. 225 at 37:2–6 (Schöneich)]. [redacted] which Mylan's expert admits is within the scope of the patents. [Doc. 225 at 179:9–13 (Hensler cross) [redacted]

[redacted] [Doc. 225 at 186:14–18 (Hensler cross) ("Q. The patent doesn't exclude any particular technique for increasing pH. For example, the patent doesn't say don't use cold manufacturing to increase pH -- increase pH. It doesn't say that, correct? A. It does not.")]. Indeed, the patent includes a specific example of a solution made and measured at 5°C. PTX-8.0005 ('802 Patent) (cl.8, ll. 60–67) ("this solution at 5°C"); *see also* [Doc. 225 at 76:6–9 (Schöneich)].

30. The patentee did not act as its own lexicographer. [Doc. 225 at 75:21–76:3 (Schöneich) ("I think they used the plain and ordinary meaning."). "Well known industry standards need not be repeated in a patent." ***Wellman Inc. v. Eastman Chem. Co.***, 642 F.3d 1355, 1367 (Fed. Cir. 2001).

31. Notably, the Asserted Claims reference "pH," not "hydronium ions", which is consistent with standard practice in the pharmaceutical industry. [Doc. 225 at 123:8–11 (Hensler) ("the patent claims themselves reference pH and not hydronium ions throughout the patents. And we also do that in the pharmaceutical industry. We live in the world of pH.")]; JTX-1.0010; JTX-2.0010.

32. pH measurements, including those of bulk solutions, have a plain and ordinary meaning in pharmaceutical manufacturing, a regulated field subject to industry standards. [Doc. 225 at 179:20–25 (Hensler) ("A POSA views these patents in the world of pH. I'm not looking at these in terms of a hydrogen ion concentration because they're not mentioned in the patent, sir.")].

ii. Specification[2]

33. A POSA reading the entirety of the patent would understand that the pH measurements in all of the examples in the patents-in-suit were done at standard temperature. [Doc. 225 at 141:22–142:3 (Hensler) ("The temperatures must be standardized. They must be -- the pH values must all be measured and reported at the same temperature.")].

34. It is undisputed that four (4) of the specifications' five (5) examples (1, 3, 4, and 5) reflected pH values as measured at standard temperature. [Doc. 225 at 76:10–13 (Schöneich cross)]; [Doc. 225 at 137:4–7 (Hensler)].

35. Examples 3 and 4 are the only examples in the specification that discuss bulk solutions having a pH of 13 or higher. [Doc. 225 at 139:9–16, 140:20–141:8 (Hensler)].

36. Dr. Hensler testified, and Dr. Schöneich conceded, that the pH values in both Example 3 and Example 4 were measured at standard temperature. [Id.]; [Doc. 225 at 76:10–13, 78:16–19 (Schöneich cross)].

37. But beginning with Example 1, each Example builds on the one before; all of them serve the same purpose of showing differential effects of pH values on the same standard-temperature scale. *See, e.g.*, [Doc. 225 at 137:4–142:15 (Hensler)].

38. Example 1 was the base case comparator for the rest of the Examples. Actelion's expert, Dr. Schöneich, agreed that a POSA reviewing Example 1 would understand that the "pH" measurement that was adjusted to 10.5 was at standard

[2] Both patents-in-suit share the same specification in all material respects. Accordingly, any discussion and citation with respect to the specification of the '802 patent applies equally to the '227 patent, and vice versa.

temperature, and the solution was then subjected to stability testing at 5 ± 1°C. [Doc. 225 at 78:21–79:3 (Schöneich cross)].

39. Example 2 then describes the first new formulation the patentee tested with a "pH" of just above 11 and draws explicit comparisons of its stability with the stability of the formulation in Example 1. [Doc. 225 at 137:18–138:13 (Hensler)]; [Doc. 225 at 78:3–13 (Schöneich cross)]; JTX-1.0006 (col. 9, ll. 30–43 (Table 5)) ("Even at pH 11.2, the data suggest better stability than the Flolan formulation (Table 2).").

40. Dr. Schöneich took the position that Example 2's solution's pH was measured at 5°C, but provided no credible explanation or support from the patent for why he believed so [Doc. 225 at 79:4-19 (Schöneich cross)]; all the patent says is that "[a] solution of epoprostenol . . . was prepared and the stability of this solution at 5°C." JTX-1.0005 (col. 8, ll. 65–67). As both experts agreed, every other example describes preparation and stability testing with substantively identical language, all with pH values measured at standard temperature. [Doc. 225 at 76:10–13 (Schöneich cross)]; [Doc. 225 at 137:4–7 (Hensler)]. In drawing comparisons between the stability of the different formulations, it would make no sense for the pH values being compared to be taken at varying temperatures. [Doc. 225 at 138:5–13, 139:2–16, 139:22–24, 140:6–15 (Hensler). Put another way, without a standardized temperature, no comparison could be made between any of the Examples. [Id.].

41. Further supporting a finding that Actelion's proposed reading of the claims is incorrect, is that assuming Example 2's pH was conducted at 5°C, Dr. Schöneich admitted then that the pH values of formulations described in Example 2 (*i.e.*, 11.2) could have been *lower* than 11 if measured at standard temperature. [Doc. 225 at 79:21–80:4

(Schöneich cross); [Doc. 225 at 138:14–20 (Hensler)]. However, the alleged invention is directed to formulations with pH *higher* than 11 (even though only formulations with a pH of 13 or higher were ultimately claimed). [Doc. 225 at 77:15–78:2, 82:13–23 (Schöneich cross)]; [Doc. 225 at 132:12–18, 133:18–23, 145:4–11 (Hensler)]. As Dr. Hensler explained, there is no basis in the specifications to conclude—nor would a POSA conclude—that Example 2's pH was measured at 5°C simply because (like the other Examples) it specifies that stability tests were carried out at 5°C. [Doc. 225 at 139:2–6 (Hensler)]; [Doc. 225 at 138:9–13 (Hensler) ("So here they're making a comparison based on the pH values. That data, as shown there in that comparison, only makes sense if those pHs were measured at the same temperature. That's the only way you can draw inference[s] from that data. Otherwise, it makes no sense.")]; [Doc. 225 at 79:1–19 (Schöneich cross)].

42. Properly understood, the specification describes all five Examples with pH values measured consistently at standard temperature. That is consistent with Dr. Hensler's testimony that the only credible reading of the specification to a POSA is that Example 2 similarly reflects pH values measured at standard temperature. [Doc. 225 at 138:5–13, 139:2–16, 139:22–24, 140:6–15 (Hensler)].

43. Likewise with respect to the data in Example 3, "[t]he only way one can draw scientifically sound conclusions from all of the data that is shown [t]here is if those pH values are taken at a standard temperature." [Doc. 225 at 139:22–24 (Hensler)]; [Doc. 225 at 140:11–15 (Hensler) ("Again, the pH values that are reported there in each of those tables have to be at a standardized temperature in order for any of this data to make

sense, in order to compare apples to apples. That's the only way that this data can be shown and made sense of.")].

44. Dr. Schöneich conceded that the pH of the bulk solution described in Example 3 was measured at standard temperature. [Doc. 225 at 76:10–13, 78:16–19 (Schöneich)]. The bulk solution described in Example 3 was a solution "containing epoprostenol and arginine [and] was adjusted to [pH] 13.0 with sodium hydroxide, and lyophilized." JTX-1.0006 (col. 9, ll. 51–53); JTX-2.0006 (col. 9, ll. 50–52). The pH was not adjusted by modification of temperature. This is the same formulation as the bulk solution described in the Asserted Claims. This further indicates to a POSA that the same standard-temperature pH scale applies throughout the patent. [Doc. 225 at 137:23–24 (Hensler) ("the patentee's attempting to show an improved stability of the active ingredient *based on* a higher *pH value*") (emphasis added)]; [Doc. 225 at 141:22-142:3 (Hensler)].

45. As to Example 4, again Dr. Schöneich conceded that the specifications' Example 4 reflected pH values measured at standard temperature. [Doc. 225 at 76:10–13, 78:16–19 (Schöneich cross)]. Included within Example 4 was the following table:

TABLE 8

Stability of several Epoprostenol prototype formulations

	Quantity (mg) of Excipient used in Formulations								
Batch #	EPP	Trehalose	Arginine	Mannitol	HES	NaCl	Glycine	Na2CO3	Bulk. Sol. pH
EPP-7	0.5		50						13
EPP-8	0.5			50		3	3.75		10.5
EPP-10	0.5		50		50				13
EPP-12	0.5							100	13
EPP-13	0.5		50		50				13
EPP-14	0.5				50				13
EPP-19	0.5			50					12
EPP-20	0.5			50					13
EPP-23	0.5			50	50				13
EPP-24	0.5			50	50				11
EPP-25	0.5		50	50					12
EPP-26	0.5		50	50					13
EPP-27	0.5		50						12
EPP-30	0.5			100			97.76		11
EPP-31	0.5			100			97.76		12
EPP-32	0.5	50					97.76		11
EPP-33	0.5	50							12
EPP-38	0.5		50						13

EPP: epoprostenol sodium;
HES: Hydroxy ethyl starch;
Bulk. Sol. pH: bulk solution pH

JTX-1.0007; JTX-2.0007. The pH values of the ***bulk solution*** in Table 8 are listed at standard temperature. [Doc. 225 at 137:4–7, 140:20–142:3 (Hensler)]; [Doc. 225 at 76:10–13, 78:16–19 (Schöneich cross)]. The EPP-8 bulk solution is "the base case for Flolan." [Doc. 225 at 141:1–4 (Hensler)]. During prosecution of the patents-in-suit, the Examiner's Notice of Allowability relied upon Tables 8 and 9 of the specification. It explained that "Applicant has amended the claims to require a composition made from a bulk solution with a pH of 13 or higher. Applicant has demonstrated unexpected results with respect to compositions made with solutions of pH 13 or higher as shown in tables 8 and 9 of the specification . . . This is an unexpected result as the prior art does not teach pH of 13 as having advantages over pH 11 or 12." JTX-3.0754. The Examiner understood the "pH of 13 or higher" in the claim was the "pH of 13 or higher *as shown in tables 8 and 9*." Dr. Hensler testified that those pH measurements were at standard temperature and

Dr. Schöneich agreed. [Doc. 225 at 137:4–7, 140:20–142:3 (Hensler)]; [Doc. 225 at 76:10–13, 78:16–19 (Schöneich cross)].

46. The fact that some aspects of the Examples concerned stability testing on reconstituted epoprostenol solutions is immaterial.[3] Epoprostenol solutions are reconstituted at room temperature. [Doc. 225 at 102:18–20 (Schöneich redirect). Not only does it follow that the pH values of bulk solutions in the Examples were measured at room temperature for that reason alone but also, the comparative nature of the Examples requires that apples be compared with apples—that is, when pH values are being used to delineate differences in formulations, those pH values must be measured at the same temperature since temperature variation impacts pH measurement. [Doc. 225 at 141:22–142:3 (Hensler)].

47. Dr. Schöneich's testimony on this issue only references to formulations with pH of 13 in the patent *except* the reference to pH of 13 in the disputed claims are measured at standard temperature. [Doc. 225 at 76:10–13, 78:16–19; Tr. 29:18–30:1 (Schöneich)]. As Dr. Hensler testified, a POSA would understand that the pH of 13 measured at standard temperature in Table 8 and "pH of 13" as identified in the claim language would refer to the same pH of 13—one measured at standard temperature. [Doc. 225 at 141:19–142:3 (Hensler)].

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[3] Indeed, as plaintiff's counsel represented to this Court at the ***Markman*** hearing, "Examples 1 to 3 with tables 2 to 7 talk about the solution stability and how the solution stability was better than Flolan even at refrigerated temperature. The patent also has data on the lyophilized material. It talks about - - and it created the lyophilized material at various pHs and ran tests and showed the stability was better at pH 13 *compared* to lower pH samples, and the lower pH samples, 10.5, 11, 12, so again we're *seeing a pattern*." [Doc. 101 at 11:23–12:6 (emphasis added)].

48. Accepting Actelion's theory would render the patent internally inconsistent and become meaningless to a POSA as it would compare pH measurements taken at different temperatures. [Doc. 225 at 141:22–142:10 (Hensler)]. In other words, it would compare apples to oranges. [Doc. 225 at 140:11–15 (Hensler) ("the pH values that are reported there in each of those tables have to be at a standardized temperature . . . in order to compare apples to apples")].

iii. Prosecution History

49. As Actelion's expert conceded, the patents-in-suit were granted as an allegedly "novel formulation of epoprostenol" which "is a more stable formulation [] [c]ontrary to the previous marketed formulation, which [] is Flolan." [Doc. 225 at 14:20–25 (Schöneich)]. In other words, throughout the prosecution history of the patents-in-suit, the Applicant distinguished the claimed invention over the prior art based on pH values in order to gain allowance. *See e.g.*, JTX-3.0699; JTX-3.0218–19. To do so, it ultimately amended claims for pH "greater than 12" to the current "pH of 13 or higher." JTX-3.0739; JTX-3.0744.

50. In the Notice of Allowance, the examiner relied upon Tables 8 and 9 from Example 4 of the specification to distinguish the claims from prior art (Watts), stating that: "Applicant has amended the claims to require a composition made from a bulk solution with a pH of 13 or higher. Applicant has demonstrated unexpected results with respect to compositions made with solutions of pH 13 or higher as shown in tables 8 and 9 of the specification . . . This is an unexpected result as the prior art does not teach pH of 13 as having advantages over pH 11 or 12." JTX-3.0754; *see also* JTX-3.0724; [Doc. 225 at 147:19–25 (Hensler)]. pH of 13 was a dividing line between patentable and unpatentable

based on prior art. The Examiner understood the "pH of 13 or higher" in the claim was the "pH of 13 or higher *as shown in tables 8 and 9*." Id.; [Doc. 225 at 76:10-13, 78:16-19 (Schöneich cross)]; [Doc. 225 at 139:9–16, 140:20–141:8 (Hensler)].

51. The only way those statements would be accurate is if they were taken at standard temperature, *i.e.*, comparing apples to apples. [Doc. 219-2 at ¶ 86]. As mentioned *supra*, this is consistent with Dr. Hensler's testimony as to how a POSA would review the examples of the patents' specifications. The observation in the prosecution history that "the pH of the bulk solution when made imparts a critical function" (JTX-3.0754) does not identify temperature of measurement and refers to unexpected results from pH of 13 formulations identified in Tables 8 and 9 of the specification, which the parties agree were measured at standard temperature.

52. The prosecution history of the patents-in-suit consistently includes comparisons of pH values which would become incomprehensible to a POSA unless those pH values denoted pH taken at standard temperature. [Doc. 225 at 139:2–6, 139:17–24, 140:11–15, 141:22–142:3 (Hensler)].

53. Dr. Hensler relied on the specification and prosecution history to inform his opinions on the plain and ordinary meaning, whereas Dr. Schöneich only pointed to generalized scientific textbooks utilized in general science courses including those taught in high school. [Doc. 225 at 96:9–11, 97:6–9 (Schöneich cross) (discussing PTX-159)]; [Doc. 225 at 156:7–11 (Hensler)]. That approach is inconsistent with a POSA in the pharmaceutical industry as "[a] person of ordinary skill in the art of pharmaceutical formulation would not look to chemical or general dictionary definitions" before "consulting pharmacological reference material", particularly the USP.

iv. Extrinsic Evidence

54. It is undisputed that a POSA at the time of the alleged invention of the patents-in-suit would be aware of, look to, and rely upon the USP, which Actelion's expert testified was "an influential document." [Doc. 225 at 47:6–10 (Schöneich cross)]; [Doc. 225 at 126:20–5 (Hensler) (POSAs would rely on USP in February 2006)]; [Doc. 225 at 48:24–49:5 (Schöneich cross) (POSAs would consult and rely on the USP in connection with pharmaceutical manufacturing)]. USP <791> states that "[m]easurements are made at 25 ± 2[°C], unless otherwise specified in the individual monograph or herein." DTX-6.002; [Doc. 225 at 126:10–14 (Hensler)]; [Doc. 225 at 52:2–5 (Schöneich cross)]. As it is undisputed that there is no individual USP monograph, or any other monograph, concerning manufacturing criteria or measurement specifications for epoprostenol or epoprostenol solutions, a POSA would rely on USP <791>. [Doc. 225 at 28:18-20 (Schöneich)]; [Doc. 225 at 171:20–22, 190:21–25 (Hensler)].

55. As Dr. Hensler testified, a POSA at the time of the invention "would view these patents through the lens of the USP [<791>]" and would have applied those standards to the manufacture of a bulk solution. [Doc. 225 at 127:6–9, 126:6–127:1 (Hensler)]. Notably, there is no reason why a POSA would have been incapable of applying USP standards in reviewing the patents-in-suit or manufacturing ANDA products formed from a bulk solution. [Doc. 225 at 27:10–13 (Hensler)]. The specification includes two references to USP—when identifying a specific ingredient in Flolan's diluent ("Water for Injection, USP"), JTX-1.0002 (col. 2, ll. 59-62), and when defining the term "self-preservation" as "the ability to pass USP preservative effectiveness test." JTX-1.0003 (col. 4, ll. 31–34). This further underscores that the POSA will be familiar with and

understand that USP pharmaceutical standards will govern the terms and substance of the patent and its claims. [Doc. 225 at 191:12–17 (Hensler)].

56. Textbooks this Court relied on in its claim construction order dated December 13, 2023, confirm that the pH scale and pH values when generally described assume SATP measurement. DTX-66.012, 019 (Kessel); DTX-67.013 (Silberberg); DTX-65.024 (Mustoe). "Neutral" pH is only defined as 7.0 at SATP. DTX-66.012, 019 (Kessel).

57. USP <791> explicitly provides for how pH is measured in manufacturing processes in the pharmaceutical field. [Doc. 225 at 127:2–9, 192:15–21 (Hensler)]. Applying a standard in pharmaceutical manufacturing makes sense because pharmaceuticals do not naturally occur at a given temperature, like blood does.

58. Mylan's ANDA states that it "follows USP standards for measuring their pH" "[a]nd that standard is the pH [] measured at 25 degrees according to that USP standard." [Doc. 225 at 121:21–24 (Hensler)]. There's no dispute that following the in-process parameters that Mylan submitted to the FDA in its tentatively approved ANDA, which by law must be followed, results in no infringement [redacted] [Doc. 225 at 58:16–18 (Schöneich cross)]; [Doc. 225 at 121:24–122:1 (Hensler) [redacted] PTX-69.0043–45. Mylan's reliance on the USP <791> is consistent with how a POSA at the time of the invention would understand the claims. [Id.]. [redacted]

which incorporates USP <791> for pH measurements [Doc. 225 at 51:5–24 (Schöneich cross)].[4] *See* [Doc. 225 at 72:17–20, 73:25–74:4 (Schöneich cross)].

59. [redacted] Actelion emphasized the parties' stipulation regarding Veletri being an embodiment of the Asserted Claims. [Doc. 225 at 11:2–7, 30:8–11, 107:1–5 (Schöneich)]. But that position supports Mylan. As Dr. Schöneich testified, [redacted]. [Doc. 225 at 69:14-70:6 (Schöneich cross) (discussing PTX-177.0024)]; [Doc. 225 at 153:4-8 (Hensler) (same)]. [redacted]

60. This was not lost on Dr. Schöneich. [redacted] [Doc. 225 at 67:10–14 (Schöneich cross) (discussing PTX-93 which is Section 3.2.P.3.3 of Actelion's NDA, Manufacturing Process Description)]. [redacted] supports Mylan's position.

61. As Dr. Schöneich concedes, [redacted] [Doc. 225 at 58:16–18 (Schöneich cross)]. Given that the Court has construed "13 or higher" to be "12.98 or higher", Mylan's

[4] While DTX-112 references "GeneraMedix", that was Actelion's predecessor. [Doc. 225 at 71:12–16 (Schöneich) (agreeing that GeneraMedix is Actelion's predecessor company)].

ANDA product will not infringe the Asserted Claims. [Id.]; [Doc. 225 at 121:24–122:1 (Hensler) [redacted]

62. In that regard, [redacted] [Doc. 225 at 71:6–11 (Schöneich cross) [redacted] [Doc. 225 at 193:7–13 (Hensler) (same)].

F. Actelion did not establish any evidence of literal infringement.

63. Even if its expert testimony can be given any weight, Actelion failed to meet its burden of establishing infringement, both literally or under the doctrine of equivalents.

i. Dr. Schöneich's litigation inspired testing was incomplete.

64. If the Court adopts Mylan's position regarding the meaning of "pH", then Dr. Schöneich's testing only of a created solution at 5°C is irrelevant. But, if the Court were to adopt Actelion's position regarding the meaning of "pH," then Mylan established that Actelion's expert failed to consider the entirety of Mylan's manufacturing process. In that case, Actelion failed to meet its burden of proving infringement. Specifically, Dr. Schöneich cherry-picked portions of Mylan's process, but ignored Mylan's Critical Process Parameter ("CPP") that states: [redacted] PTX-7.0005; [Doc. 225 at 84:23–85:8 (Schöneich cross)]. [redacted] PTX-7.0005. [redacted]

[redacted] [Doc. 225 at 87:3–6 (Schöneich cross)]

65. Dr. Schöneich did not replicate the last step of Mylan's bulk solution manufacturing process in his testing. [Doc. 225 at 85:9-13 (Schöneich cross) [redacted]]; [Doc. 225 at 114:5–13 (Schöneich recross) (acknowledging his testing did not account for last critical step)]. Dr. Schöneich first testified that he did not consider the third CPP that accounted for 1/3 of Mylan's total manufacturing process before lyophilization because "we don't know how long [the bulk solution] sits there[.]" [Doc. 225 at 87:3–10 (Schöneich cross)].

66. But cross examination bore out that Dr. Schöneich did, in fact, know how long Mylan's bulk solution sat [redacted]. The batch manufacturing records, which he admittedly reviewed in forming his opinions [Doc. 225 at 90:1–3], showed that the third step [redacted] PTX-86.0119 [redacted]); [Doc. 225 at 90:13–25 (Schöneich cross) (conceding same)]; PTX-82.0119 [redacted]; [Doc. 225 at 91:9–19 (Schöneich cross) (conceding same)]; PTX-83.0119 [redacted]; [Doc. 225 at 91:21–92:4 (Schöneich cross) (conceding same)]; PTX-84.0120 [redacted]; [Doc. 225 at 92:8–14 (Schöneich cross) (conceding same)]; PTX-85.0120 [redacted]; [Doc. 225 at 92:21–25 (Schöneich cross) (conceding same)]; PTX-92.0123

[redacted]; [Doc. 225 at 93:5–12 (Schöneich cross) (conceding same)]. Dr. Schöneich's testing of his simulated Mylan bulk solution showed that at 25°C, the pH of Mylan's solution would be [redacted]—***not*** 13 or higher. [Doc. 225 at 67:5–9 (Schöneich cross)].

67. Actelion's attempt at rehabilitating Dr. Schöneich during re-direct ignored the record evidence. [Doc. 225 at 101:4–18 (Schöneich redirect)]. Actelion's counsel directed Dr. Schöneich to a portion of Mylan's batch record directed to *lyophilization* but as both experts agreed "bulk solution [] precedes the lyophilization step." [Doc. 225 at 131:16–17 (Hensler); [Doc. 225 at 18:8–11 (Schöneich) (describing process of filling bulk solution into vials prior to lyophilization)]; [Doc. 225 at 83:20–23 (Schöneich) [redacted]]; [Doc. 225 at 7:9–11 (Schöneich) [redacted].

68. But even there, the portion of Mylan's Batch Record (PTX-92) that counsel directed Dr. Schöneich to argue that there is a [redacted] [Doc. 225 at 101:14–18 (Schöneich redirect) (discussing PTX-92)]. [redacted]

[redacted]

PTX-92.0109. The same is true for the rest of Mylan's Exhibit Batch Records. *See* PTX-82.0105 (same); PTX-83.0105 (same); PTX-84.0106 (same); PTX-85.0106 (same); PTX-86.0105 (same); *see also* PTX-69.0041 [redacted]; PTX-71.0080.

69. Even Dr. Schöneich disagreed with Actelion's counsel on his re-direct when he testified that [redacted] [Doc. 225 at 100:3–9 (Schöneich redirect) [redacted]]. [redacted] [Doc. 225 at 95:12–16 (Schöneich cross) (discussing claim 1 [redacted]]; *see* [Doc. 225 at 112:16–24 (Schöneich redirect) [redacted]]; [Doc. 76 at 1 ("of the bulk solution *from which the drug product is formed*") (emphasis added)]; [Doc. 225 at 159:7–9 (Hensler) ("The claims recite a composition formed from a bulk solution.")].

70. As such, even if Actelion's claim construction was adopted (which, it is not), Actelion failed to meet its burden in proving infringement because Dr. Schöneich did not test Mylan's bulk solution at its "actual" or "operating" temperature prior to lyophilization, under his own theory. In other words, Actelion presented no evidence of the pH of the bulk

solution at the "operating temperature" when the claimed "lyophilized pharmaceutical composition" is in fact "formed from" it.

G. Actelion did not meet its burden to establish infringement under the doctrine of equivalents.

71. Actelion cannot ensnare Mylan's ANDA product via the doctrine of equivalents.

i. Actelion is precluded from asserting doctrine of equivalents for multiple, independent reasons.

1. The patent discloses but does not claim pHs lower than 13.

72. The specifications of the patents-in-suit disclose unclaimed subject matter with such specificity that a POSA could identify subject matter that is disclosed but not claimed. [Doc. 225 at 144:15–25 (Hensler)]; [Doc. 225 at 82:13–16 (Schöneich cross)].

73. The specifications disclose four (4) alternatives but ultimately the patentee chose to only claim one (1) of those alternatives, namely, a pH of 13 or higher. [Doc. 225 at 145:4–11 (Hensler)].

74. As Dr. Hensler testified, a POSA reading the specifications of the patents-in-suit would identify that the patentee disclosed, but did not claim, the subject matter of: (i) bulk solution pHs between 12.5 and 12.98; (ii) bulk solution pHs between 11 and 12.98; and (iii) bulk solution pHs between 12 to 12.98. [Doc. 225 at 145:12–146:5 (Hensler)]; *see* JTX-1.0004 (col. 5, ll. 39–43); JTX-1.0004 (col. 5, ll. 35–38).

75. Actelion did not offer any testimony or evidence to rebut the testimony of Dr. Hensler with respect to the factual underpinnings of the disclosure dedication doctrine.

2. The prosecution history estoppel precludes infringement.

76. The patentee narrowed its claims during prosecution for the purpose of obtaining allowance. [Doc. 225 at 146:12–13 (Hensler) ("The patentee did, in fact, narrow their claims during the prosecution history, yes.")]. The patentee initially "tried to win approval for pHs greater than 11" which "was rejected by the examiner." [Doc. 225 at 146:24–147:1 (Hensler)]; JTX-3.0008; JTX-3.0191.

77. The patentee then attempted to gain allowance with bulk solutions of pH greater than 12, but that was also rejected so the patentee went straight to the pH of 13 or higher language used in the claims. [Doc. 225 at 147:1–3 (Hensler)]; JTX-3.0656; JTX-3.0739.

78. As stated above, the examiner only allowed the claims with a "pH of 13 or higher" as being unexpectedly superior to the prior art. *See supra* ¶¶ 45, 50. Accordingly, the amendment narrowing the claim to a pH of 13 or higher is central to the purported equivalent, not tangential. COL[5] ¶¶151–152; [Doc. 225 at 147:9–25 (Hensler)].

79. Actelion cannot now regain, through litigation, subject matter it relinquished through prosecution of the patents-in-suit. COL ¶ 148.

80. Actelion bears the burden of refuting the presumption of surrender. COL ¶ 151. Dr. Schöneich did not consider the doctrine.

81. As Dr. Hensler credibly testified, the alleged equivalent (12.5–12.8) could reasonably have been described at the time of the amendment. [Doc. 225 at 147:4–8 (Hensler)]. Dr. Hensler further testified that the purpose of the amendments during prosecution were directly relevant to the alleged equivalent that was given up, and not

[5] "COL" refers to the "**CONCLUSIONS OF LAW**" section.

tangential. [Doc. 225 at 147:9–18 (Hensler)]. Similarly, Dr. Hensler testified that the alleged equivalent was clearly foreseeable at the time of the amendment. [Doc. 225 at 148:3–11 (Hensler)]. Dr. Schöneich did not offer any testimony to the contrary.

ii. Even if Actelion was not barred, it failed to meet its burden of proof as to doctrine of equivalents.

82. Dr. Schöneich engaged in a legally improper doctrine of equivalents infringement analysis, by comparing generally Mylan's ANDA product with Veletri, rather than to the Asserted Claims on a limitation-by-limitation basis.

83. Dr. Schöneich only offered an opinion as to infringement based on the function-way-result test.[6] [Doc. 225 at 39:23-40:7 (Schöneich)].

84. Rather than applying the proper element-by-element analysis, Dr. Schöneich equated "bioequivalence" with "equivalents" with respect to infringement. [Doc. 225 at 35:10–36:16 (Schöneich)]. This is an improper analysis. COL ¶ 154. As Dr. Schöneich admitted, it is his understanding that a generic is required to be bioequivalent by law. [Doc. 225 at 42:6–14 (Schöneich cross)]. In other words, if Dr. Schöneich's doctrine of equivalents analysis were to be accepted and applied in ANDA cases, no alternative to a patented medicine could ever be offered to the public during the life of a patent. COL ¶ 154.

85. Dr. Schöneich's opinion was based on an impermissibly high level of generality, applying the function-way-result test to *Mylan's bulk solution* and **not** the "pH

[6] Dr. Schöneich is limited, pursuant to Federal Rule of Civil Procedure 26, to only opine on those opinions properly disclosed during discovery. [Doc. 225 at 80:23–81:3 (Glasser objection)]. The case law with respect to function-way-result indicates that it is more appropriate in mechanical cases, whereas the unconsidered "insubstantial differences test" is more appropriate in chemical cases. Actelion cannot post-trial argue infringement under the substantial differences test. COL ¶ 153; PTO at 25, fn.13.

of 13 or higher" limitation. [Doc. 225 at 39:23–40:7 (Schöneich)]. Dr. Schöneich testified that temperature affects pH by modifying the behavior of water. [Doc. 225 at 22:3–9, 37:7–14 (Schöneich) ("At cooler temperatures, fewer molecules of water break up to get hydrogen ions. At higher temperature, more water molecules break up to create hydrogen ions.")]. Dr. Schöneich also failed to consider the "all elements rule" of claim vitiation. [Doc. 225 at 97:23–25 (Schöneich) (admitting he does not know of the "all-elements" rule)].

86. Notably, Dr. Schöneich didn't even have conviction in his *own* analysis. He testified in response to his counsel's question that the hydrogen ion concentration, he "think[s] would be identical ***if they infringe***." [Doc. 225 at 38:14–20 (Schöneich) (emphasis added)].

H. Actelion's position with respect to pH would render the Asserted Claims indefinite.

87. As Dr. Hensler credibly testified, the claims are clear that the "pH" limitation should be read to have its plain and ordinary meaning of standard temperature pursuant to the USP. [Doc. 225 at 127:6–9, 155:5–15 (Hensler)]. But, should Dr. Schöneich's position be accepted (which it is not), there would be "a case where you have two potential means in which to do it [a]nd depending on which mean you use, you'll end up [at] different results." [Doc. 225 at 122:8–10 (Hensler)].

88. If the claim specifies a substance (bulk solution) and pH value (13 or higher) but the patent leaves the temperature of pH measurement an open variable, it does not reasonably inform a POSA about the scope of what is claimed, and therefore would be invalid as indefinite. [Doc. 225 at 148:12–149:1 (Hensler)].

89. Under Actelion's theory, different manufacturers may use different standards of measurement. [Doc. 225 at 122:3–14, 148:23–149:1 (Hensler)]. Without intrinsic guidance from the patent, one manufacturer may rely on USP, while another could follow Dr. Schöneich's approach and measure at "operating temperature." The differing approaches could lead to some measurements with infringing values and others with non-infringing values. [Doc. 225 at 149:5–11, 148:16–149:1 (Hensler)].

90. This exemplifies a second issue with Actelion's position—what the "operating temperature" of the bulk solution actually is. As previously noted, the claim language does not specify *when* or at what *stage* the pH of the bulk solution should be assessed. It states only that a lyophilized composition is "formed from a bulk solution having a pH of 13 or higher." JTX-1.0010; JTX-2.0010. The specification likewise only indicates that the pH is adjusted *before lyophilization*. *See* JTX-1.0006, JTX-2.0006 ("[T]he pH of the solution containing epoprostenol and arginine was adjusted to 13.0 with sodium hydroxide, and lyophilized."). Dr. Schöneich did not provide a clear, applicable definition of "operating temperature," instead using it in contexts that appeared to refer to different things. [Doc. 225 at 29:18–30:1, 38:5–7, 53:14–19, 54:1–4, 54:21–25 (Schöneich)].

91. Different manufacturers will have different processes and temperature conditions— [redacted]. There are any number of conditions the bulk solution may be exposed to before lyophilization. [redacted] [Doc. 225 at 150:8–19, 151:2–10, 153:1–23 (Hensler); 61:24–62:10 (Schöneich cross)]. [redacted]. PTX-7.0005; [Doc. 225 at

84:23–85:8 (Schöneich cross)]. If temperature of pH measurement is not standardized, a bulk solution (like [redacted]) may have varying temperatures, engendering further uncertainty as to when pH measurements should be made in determining whether a product infringes or not. Standardization remedies this concern—but if Actelion's non-standardized position were adopted, the claims would fail to inform a POSA with reasonable certainty the scope of the purported invention. [Doc. 225 at 122:3–14, 149:5–11, 148:16–25 (Hensler)].

92. Actelion's theory fails to specify the measurement, technique, or conditions for assessing whether a given bulk solution infringes. That, in turn, would not provide adequate guidance to a POSA.

93. Actelion did not provide any testimony or evidence rebutting Mylan's indefiniteness contention.

II. CONCLUSIONS OF LAW

A. Summary

94. This case boils down to the "plain and ordinary meaning" of the term "pH of 13" as of the priority date (of February 3, 2006). And there, the sole question is whether pH as claimed is measured at standard temperature, or at an unspecified temperature dependent on variable manufacturing conditions of a given accused product.

95. The intrinsic evidence compels the right answer. pH values are measured at standard temperature (25 ± 2°C). That plain and ordinary meaning flows directly from the patents' specifications and Examples. Yet Actelion, which bears the burden of proof, hardly addressed the intrinsic evidence in its case-in-chief. Its expert did not offer direct

testimony on the specification, nor did it cross Mylan's expert on key statements made therein.

96. The specification is usually dispositive of the meaning of a disputed term. *See* ***Phillips v. AWH Corp.***, 415 F.3d 1303, 1315 (Fed. Cir. 2005) (*en banc*). Here, it is fatal to Actelion's position. The evidence established a POSA would understand the patent as a whole to be consistently referring to pH values at standard temperature. First and foremost, the specification identifies pH of greater than 7 as "alkaline" or "basic," *something only true at standard temperature*. FOF[7] ¶ 17. This establishes a baseline for all pH values reported (and claimed) in the patents—a POSA would have understood them to be provided on the same scale where pH>7 is alkaline, pH of 7 is neutral, and pH<7 is acid (*i.e.*, at standard temperature).

97. The conclusion compelled by the intrinsic evidence is buttressed by the extrinsic. As POSAs in the pharmaceutical industry understand, the United States Pharmacopeia (USP) provides that pH is measured at 25 ± 2°C unless a different temperature for measurement is specified in a monograph. Consistent with that understanding, both [redacted] FOF ¶ 58; PTX-69.0043–45; DTX-112.001; *See* ***Wellman Inc. v. Eastman Chemical Co.***, 642 F.3d 1355, 1367 (Fed. Cir. 2001) ("Well known industry standards need not be repeated in a patent.").

98. Because it was undisputed that Mylan's ANDA product has a bulk solution pH of lower than 12.98 when measured at standard temperature, Mylan does not literally infringe the asserted claims.

[7] "FOF" refers to the "**FINDINGS OF FACT**" section.

99. Actelion further failed to carry its burden on infringement under the doctrine of equivalents. First, as a matter of law, Actelion is precluded from relying on the doctrine of equivalents by (1) the doctrine of disclosure dedication and (2) the doctrine of prosecution history estoppel. Each provides an independent basis to bar Actelion from proving Mylan's ANDA product infringes under the doctrine of equivalents. Even putting those aside, Actelion did not meet its burden of proving equivalence because its expert did not provide testimony specifically directed to the disputed limitation as is required for any infringement determination. In fact, its expert had never heard of the "all elements rule." FOF ¶ 85. Accordingly, Mylan does not infringe under the doctrine of equivalents.

100. Finally, if Actelion's reading of the patent were somehow correct, the asserted claims would be invalid for indefiniteness because they would not and could not account for different forms of measurement and differences in manufacturing conditions. This underscores that a reading of the patent in which pH values consistently refer to pH as measured on a standard-temperature scale is the correct one.

A. Mylan's ANDA product does not infringe because a POSA understands "pH of 13 to be measured at standard temperature.

101. "An infringement analysis has two steps. First, the court construes the asserted claims. Claim construction is a question of law that may involve underlying factual questions. . . . Second, the court determines whether the accused product meets each limitation of the claim as construed, which is a question of fact . . . review[ed] for clear error." ***Indivior Inc. v. Dr. Reddy's Lab'ys, S.A.***, 930 F.3d 1325, 1336 (Fed. Cir. 2019) (citations omitted). "[A] dependent claim necessarily cannot be infringed if the independent claim is not infringed." ***Cognex Corp. v. Int'l Trade Comm'n***, 550 Fed.App'x 876, 881

(Fed. Cir. 2013). "[I]nfringement is determined on the basis of the claims, not on the basis of a comparison with the patentee's commercial embodiment . . . ." ***Int'l Visual Corp. v. Crown Metal Mfg. Co.***, 991 F.2d 768, 772 (Fed. Cir. 1993) (quotation marks omitted).

i. A dispute as to the plain and ordinary meaning of "pH of 13" remains.

102. The parties' sole dispute implicates how the limitation "pH of 13 or higher" should be understood and applied. This, in turn, implicates the plain and ordinary meaning of the term "pH" to a POSA. Mylan contends that a POSA, reading the claim term in the context of the patent and in view of well-known standards applicable to the pharmaceutical industry, understands references to pH that do not specify a temperature for measurement denote pH value assessed at standard ambient temperature and pressure (SATP)—which, in relevant part, specifies a temperature of 25 ± 2°C. Actelion contends that "pH of 13" means a pH of 13 as measured at whatever the "operating" or "actual temperature" of the "bulk solution" is, because a POSA will understand "pH" merely to denote a "hydrogen ion concentration."

103. Inasmuch as this is a claim construction dispute, it is axiomatic that "a district court may engage in claim construction during various phases of litigation, not just in a ***Markman*** order." ***AstraZeneca AB v. Mylan Pharms., Inc.***, 2022 WL 17178691, at *9 (N.D.W. Va. Nov. 23, 2022) (Bailey, J.) (quoting ***Conoco, Inc. v. Energy & Envtl Int'l, L.C.***, 460 F.3d 1349, 1359 (Fed. Cir. 2006)). "[T]he Federal Circuit has repeatedly upheld a district court's decision to revisit claim construction as the case progresses, including at trial." ***Chemours Co. FC, LLC v. Daikin Indus., Ltd.***, 2022 WL 2753636, at *2

(D. Del. June 30, 2022). Thus, "in cases tried to the bench," it is appropriate to address claim construction in a post-trial opinion where "the Court's [earlier] construction did not resolve the parties' dispute." ***Trimed, Inc. v. Arthrex, Inc.***, 2021 WL 1174532, at *6 (D. Del. Mar. 29, 2021).

104. The Court's prior claim construction order does not resolve the parties' dispute. The Court's order did not define "pH of 13" in terms of hydrogen ion concentration, or as any particular hydrogen ion concentration. This makes sense, as this Court was not asked to construe "pH of 13" as "hydrogen ion concentration." Rather, in the course of reasoning that pH has two implied significant digits, this Court observed that a table in the Mustoe reference equated "pH of 13" and a hydrogen ion concentration of "0.000 000 000 0001." [Doc. 207 at 20 (citing PTX-95 at 23)]. But the Mustoe table depicted pH values and concentration equivalents *as measured at standard temperature* because it defined "neutral" pH as "pH of 7." [Id.]; FOF ¶ 18. Indeed, all the extrinsic sources upon which the Court relied made clear that the standard way to express pH when no temperature is specified is at SATP. FOF ¶ 18. And as both experts at trial acknowledged, temperature has a direct impact on both pH and hydrogen ion concentration. FOF ¶ 17.

105. The question for this Court is therefore not to determine a hydrogen ion concentration of Mylan's product in a manner untethered to the claims. The question is whether the patent's reference to "pH of 13" in the claims *means pH measured at standard temperature* or at some other temperature.

106. Further, regardless of whether the temperature of measurement is deemed a matter of claim construction, the Court must still decide the issue. Actelion's proposed "bulk solution operating temperature" understanding of pH taken at non-standard temperatures does not control by default. There is "a 'heavy presumption' that a claim term carries its ordinary and customary meaning." ***CCS Fitness, Inc. v. Brunswick Corp.***, 288 F.3d 1359, 1366 (Fed. Cir. 2002). The plain and ordinary meaning of a term or a phrase is a proper subject for expert testimony even if it does not amount to claim construction, because a POSA's understanding of a term is a factual question. *See, e.g.*, ***Apple, Inc. v. Samsung Elecs. Co.***, 2014 WL 660857, at *3 (N.D. Cal. Feb. 20, 2014) (Koh, J.). The temperature at which pH is tested also goes to the relevant *test for infringement*, which is also an issue for the Court as fact-finder. *See, e.g.*, ***Lazare Kaplan Int'l, Inc. v. Photoscribe Techs., Inc.***, 628 F.3d 1359, 1376 (Fed. Cir. 2010).

107. Whether characterized as a matter of law or a matter of fact, the term "pH of 13 or higher" is understood by a POSA to reflect pH as measured at standard temperature. That not only comports with the intrinsic and extrinsic evidence, but also aligns with well-reasoned authority. *See* ***Dow Chem. Co. v. Halliburton Co.***, 631 F.Supp. 666, 688–89 (N.D. Miss. 1985) ("The pH is normally measured at room temperature, and a measurement not showing a temperature would connote measurement at room temperature to one skilled in the art."), *aff'd*, 790 F.2d 93 (Fed. Cir. 1986).

B. The term "pH of 13 or higher" in the context of the claims at issue refers to pH measured at standard temperature.

108. A term must be "define[d] . . . in a manner consistent with the scientific and technical context in which it is used in the patent." ***AFG Indus., Inc. v. Cardinal IG Co.***,

239 F.3d 1239, 1248 (Fed. Cir. 2001). "[T]he descriptions in patents are not addressed to the public generally, to lawyers or to judges, but to those skilled in the art to which the invention pertains or with which it is most nearly connected." ***In re Fetzima***, 2021 WL 2349981, at *5 (D.N.J. June 8, 2021) (quotation marks omitted). Actelion concedes that it did not "act as its own lexicographer," ***Hill-Rom Servs. v. Stryker Corp.***, 755 F.3d 1367, 1371 (Fed. Cir. 2014), with respect to "pH of 13." FOF ¶ 30.

109. "Well known industry standards need not be repeated in a patent." ***Wellman***, 642 F.3d at 1367 ("[T]he record shows that a person of ordinary skill in the art in this field would follow standard industry guidance for conditioning plastics . . . ."). In ***Wellman***, for example, the court credited testimony that a "person of skill in the art would have interpreted the [] patents in view of the internationally recognized 1997 ISO," and "[t]he record suggest[ed] no reason that a person of skill in the art would have been incapable of applying those . . . standards to the claimed invention to achieve consistent, repeatable . . . measurements." ***Id.*** at 1368.

110. One such bedrock standard for pharmaceuticals is the United States Pharmacopeia (USP), which this Court and other courts have found to be a "well-recognized standard in the pharmaceutical industry [that] would be familiar to a skilled artisan." [Doc. 207 at 24]; *see, e.g.*, ***Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.***, 288 F.Supp.2d 562, 574 (S.D.N.Y. 2003); *see also* ***id.*** at 575 ("A person of ordinary skill in the art of pharmaceutical formulation would not look to chemical or general dictionary definitions of the individual components of the compound term 'hydrogenated vegetable oil' before consulting pharmacological reference material that contained

definitions of the entire term."). Among other things, USP defines processes and standards that practitioners in the pharmaceutical industry use during manufacturing. FOF ¶ 20.

111. The USP standard applicable to pH measurement in pharmaceutical manufacturing is USP <791>. FOF ¶ 22. According to USP <791>, "measurements are made at 25 ± 2[°C], unless otherwise specified in the individual monograph or herein." DTX-6.002; FOF ¶ 22. It was undisputed that there is no individual USP monograph concerning manufacturing criteria or measurement specifications for epoprostenol or epoprostenol solutions. FOF ¶ 22. And the only other portion of the USP (the "herein") discussing pH is related to calibration of pH meters in the event an individual monograph specifies taking pH measurements at temperatures other than 25 ± 2°C. FOF ¶ 22.

112. The patents do not specify a temperature for pH measurement. FOF ¶ 25. As discussed below, the intrinsic and extrinsic evidence compels the conclusion that they use a single standard benchmark and uniformly describe pH values as measured at standard temperature, namely 25 ± 2°C, consistent with the USP standard for pH measurement. Accordingly, the claim language "formed from a bulk solution having a pH of 13 or higher" refers to a pH of 12.98 or higher as measured at 25 ± 2°C.

i. Intrinsic Evidence supports a conclusion that "pH" in the context of the patents refers to pH as measured at standard temperature.

113. The patents' specifications and prosecution history confirm that the claim language "pH of 13" refers to pH measured at standard temperature. A contrary reading would render the patent internally inconsistent and of negligible practical use to a POSA because it would compare pH values taken at different temperatures—apples and oranges.

Although the specification is relevant to both the legal question of claim construction and the factual question of "plain and ordinary meaning," Actelion did not elicit any testimony or present any evidence regarding the specification. Actelion's proposed "operational temperature" standard, which would redefine "pH" as "hydrogen ion concentration" and ignore the impact of temperature on both, cannot be squared with the evidence.

114. First, as noted, the patent specification states that "[t]he composition of the present invention contains epoprostenol, or a salt thereof, and an alkalinizing agent," and defines "[a]n alkalinizing agent, as used herein, [as] an agent that provides *alkaline environment (pH>7)* when epoprostenol is dissolved in water along with the alkalinizing agent." JTX-1.0003 (col. 4, ll. 62-64) (emphasis added); JTX-2.0004 (col. 5, ll. 3–5) (same). Thus, the patent specifically defines an "alkaline environment" as "pH>7." Id.; FOF ¶ 17. In other words, the specification defines a "neutral" pH as "7." Id.

115. It was undisputed at trial that these definitions of neutral and alkaline environment are only true at *standard temperature*. FOF ¶¶ 17–18. At different temperatures, "neutral" is *not* pH 7.0; it may be higher or lower, which necessarily results in an alkaline environment that is *not* "pH>7." FOF ¶ 17; *see also* ***Dow Chem.***, 631 F.Supp. 666. The Court's prior claim-construction order recognized that pH values described as 7, 7.0, or 7.00 are considered "neutral," *see* [Doc. 207 at 22], and credited evidence showing that this is only true at standard temperature. *See* [Doc. 207 at 22 (citing [Doc. 198-1 at 775, 797])].

116. The specification therefore unambiguously signals to a POSA that a reference to a "pH" value will be on the same scale on which "7" is a *neutral* pH and pH

"greater than 7" is *alkaline*. FOF ¶¶ 17–18. In effect, the patent provides a yardstick for measuring all of the pH values identified therein. Because the claim language does not specify a different temperature for measuring the "bulk solution," a POSA will understand the "pH of 13" at issue to be on the *same scale* as the scale on which "pH>7" represents an alkaline, or basic, environment. It necessarily follows that "pH of 13" in the claim refers to a pH of 13 at 25 ± 2°C. Concluding that the patent's references to pH are consistent and imply a standard-temperature scale accords with this Court's previous ruling that pharmaceutical industry conventions (there, applying decimals) are implicit in the patent. [Doc. 207 at 24].

117. Second, the specification and prosecution history include numerous comparisons of pH values that would not make sense or convey comprehensible information to a POSA unless their references to pH denoted pH measured consistently at standard temperature. Actelion did not present any evidence, testimony, or justification for a reading of the patent to provide comparisons on different scales at different temperatures. Indeed, none of Actelion's evidence meaningfully addressed the perspective of a POSA *who had read the entire patent* because Actelion did not proffer substantive affirmative testimony on the specification. *Cf.* ***Fetzima***, 2021 WL 2349981, at *5 ("Defendants do not provide any evidence to show that *a POSA reading the patent as a whole* would understand the dosage descriptions differently from the industry practice [of following USP]." (emphasis added)).

118. The Examples bear this out. Each Example builds on the one before; all of them serving the same purpose of showing differential effects of pH values on the same

standard-temperature scale. The specification begins with Example 1, a simulated prior-art Flolan formulation with pH of 10.5 at standard temperature. FOF ¶ 38. Example 2 introduces a new formulation adjusted by the patentee to a pH of 11.2, with the express purpose of comparing its stability to that of Flolan. Id. The parties agree Example 1's pH was measured at standard temperature. FOF ¶¶ 34, 41. The only way the patentee's comparison of a pH-11.2 formulation to a pH-10.5 formulation makes sense is if both pH values are measured at the same temperature. FOF ¶ 40. That is because temperature and pH have an undisputed relationship—the lower the temperature, the higher the pH. FOF ¶ 17. pH must be standardized across the measurements to inform a POSA how pH impacts stability of different formulations; otherwise, there would be an additional variable and the patent would not be comparing "apples to apples."

119. Examples 3 and 4 confirm pH is measured at standard temperature. Example 3 describes a bulk solution whose pH is adjusted to 13.0—undisputedly measured at standard temperature—with sodium hydroxide and then lyophilized. FOF ¶¶ 34–35. This formulation, too, is compared to Flolan. FOF ¶¶ 44–45; JTX-1.0006 (col. 9, l. 45 – col. 10, l. 54); JTX-2.0006 (col. 9, l. 45 – col. 10, l. 54). Notably, the bulk solution and pH of Example 3 are *the same* as the bulk solution and pH described in Claim 1 of the '802 patent. Id.

120. Example 4 provides a table of sample formulations whose bulk solution pH values range from 10.5 to 13—all of which, Actelion concedes, were measured at standard temperature. FOF ¶ 45. It was Example 4, and specifically the Tables therein, that led the U.S. Patent and Trademark Office to issue a Notice of Allowance for claims incorporating a bulk solution having a pH of 13 or higher. Id. When the claims at issue were ultimately

allowed based on sample formulations whose pH was undisputedly measured at standard temperature, the only reading that harmonizes the claims with the specification and prosecution history is that the claims refer to pH values at standard temperature, too.

121. Mylan's evidentiary presentation and cross-examination showed it was undisputed that four (4) of the specification's five (5) Examples (1, 3, 4, and 5) reflected pH values as measured at standard temperature. FOF ¶ 34. The parties disputed whether Example 2 was measured at standard temperature. FOF ¶¶ 40–41.

122. The only credible reading of the specification is that Example 2 reflects pH values measured at standard temperature. Critically, Example 1 provides the baseline comparator for the rest of the Examples—a simulated Flolan formulation at a "pH" of 10.5. FOF ¶ 38. With respect to Example 1, a POSA reading the specification would understand that the "pH" measurement that was adjusted to 10.5 was at standard temperature, and the solution was then subjected to stability testing at 5 ± 1°C (Table 2). Id. Actelion's expert, Dr. Schöneich, agreed. Id.

123. Example 2 then describes the first new formulation the patentee tested with a "pH" of just above 11 and draws *explicit* comparisons of its stability with the stability of the Example 1 formulation. FOF ¶ 38. Again, the stability test is conducted at 5 ± 1°C, and the patentee concluded that "[e]ven at pH 11.2, the data suggest better stability than the Flolan formulation (Table 2)." JTX-1.0006, (col. 9, ll. 30-43 (Table 5)). The specification is, for the first time, showing the superiority of a higher-pH formulation to the known Flolan formulation. To convey to a POSA that a (new) 11.2 pH solution had clear advantages over the (old) Flolan 10.5 pH solution, they had to be measured against the same yardstick. FOF ¶¶ 40–41.

124. Dr. Schöneich took the position that the Example 2 solution's pH was measured at 5°C, but provided no credible explanation or support from the patent for why he believed so. FOF ¶ 40. All the patent says is that "[a] solution of epoprostenol . . . was prepared and the stability of this solution at 5°C. was determined." JTX-1.0005 (col. 8, ll. 65–67). Dr. Schöneich's reading is not credible. As both experts agreed, every other Example describes preparation and stability testing with substantively identical language, all with pH values measured at standard temperature. FOF ¶ 40. In drawing comparisons between the stability of the different formulations, including when the stability studies are conducted at different temperatures, it would make no sense for the pH values being compared to be taken at varying temperatures. Id. Furthermore, Dr. Schöneich admitted that under his theory, the pH values of formulations described in Example 2 could have been *lower* than 11 if measured at standard temperature. FOF ¶ 41 (citing [Doc. 225 at 79:21–80:4] ("Q. [I]f I increase the temperature from 5 degrees to 25, would that 11.2 go up or down? A. 11.2—well, this is the epoprostenol, but I think it would go down. . . . Q. Is it possible it would go down below 11? A. It's possible.")).

125. However, the invention is directed to formulations with pH *higher* than 11, even though only formulations with a pH of 13 or higher were ultimately claimed. FOF ¶ 41. As Dr. Hensler explained, there is no basis in the specification to conclude—nor would a POSA conclude—that Example 2's pH was measured at 5°C simply because (like the other Examples) it specifies that stability tests were carried out at 5°C. FOF ¶ 41. Properly understood, the specification describes all five Examples with pH values measured consistently at standard temperature. That is consistent with Dr. Hensler's testimony that the only credible reading of the specification to a POSA is that Example 2 similarly reflects

pH values measured at standard temperature. [Doc. 225 at 138:5–13, 139:2–16, 139:22–24, 140:6–15 (Hensler)].

126. The fact that all of the specification's examples compare pH values at standard temperature and the patent only discusses modifying pH by addition of alkaline substances (as opposed to by modifying temperature of the solution) strongly supports a construction whereby "pH" in the claim refers to pH at standard temperature. *See, e.g.*, ***Renishaw PLC v. Marposs Societa' per Azioni***, 158 F.3d 1243, 1250 (Fed. Cir. 1998) ("The construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction.").

127. Furthermore, Dr. Schöneich conceded that the pH of the solution described in Example 3 was measured at standard temperature. FOF ¶ 44. The solution described in Example 3 was a solution "containing *epoprostenol and arginine* [and] *was adjusted to [pH] 13.0 with sodium hydroxide*, and lyophilized." JTX-1.0006 (col. 9, ll. 51–53) (emphasis added); JTX-2.0006 (col. 9, ll. 50–52) (same). It was not adjusted by modification of temperature. This is an identical bulk solution to the one described in Claim 1 of the '802 patent. This further indicates to a POSA that the same standard-temperature pH scale applies throughout the patent, including in the claims. FOF ¶ 44.

128. There is more. Dr. Schöneich conceded that the specification's Example 4 reflected bulk solution pH values measured at standard temperature. FOF ¶ 45. Example 4 included this table:

TABLE 8

Stability of several Epoprostenol prototype formulations

	Quantity (mg) of Excipient used in Formulations								
Batch #	EPP	Trehalose	Arginine	Mannitol	HES	NaCl	Glycine	Na2CO3	Bulk. Sol. pH
EPP-7	0.5		50						13
EPP-8	0.5			50		3	3.75		10.5
EPP-10	0.5		50		50				13
EPP-12	0.5							100	13
EPP-13	0.5		50		50				13
EPP-14	0.5				50				13
EPP-19	0.5			50					12
EPP-20	0.5			50					13
EPP-23	0.5			50	50				13
EPP-24	0.5			50	50				11
EPP-25	0.5		50	50					12
EPP-26	0.5		50	50					13
EPP-27	0.5		50						12
EPP-30	0.5			100			97.76		11
EPP-31	0.5			100			97.76		12
EPP-32	0.5	50					97.76		11
EPP-33	0.5	50							12
EPP-38	0.5		50						13

EPP: epoprostenol sodium;
HES: Hydroxy ethyl starch;
Bulk. Sol. pH: bulk solution pH

Critically, the Examiner's Notice of Allowability relied upon Tables 8 and 9 of the specification. It explained that "Applicant has amended the claims to require a composition made from a bulk solution with a pH of 13 or higher. Applicant has demonstrated unexpected results with respect to compositions made with solutions of pH 13 or higher as shown in tables 8 and 9 of the specification . . . This is an unexpected result as the prior art does not teach pH of 13 as having advantages over pH 11 or 12." JTX-3.0754. The Examiner understood the "pH of 13 or higher" in the claim was the "pH of 13 or higher *as shown in tables 8 and 9*." As Dr. Hensler credibly testified and Dr. Schöneich admitted, those pH measurements were at standard temperature. FOF ¶ 45.

129. The fact that some aspects of the Examples concerned stability testing on reconstituted epoprostenol solutions is immaterial. Epoprostenol solutions are reconstituted at room temperature. FOF ¶ 46 However, it does not follow that the pH

values of bulk solutions in the Examples were *only* measured at room temperature *for that reason*. Instead, the comparative nature of the Examples requires that apples be compared with apples—that is, when pH values are being used to define differences in formulations, those pH values must be measured at the same temperature since temperature variation impacts pH measurement.

130. Dr. Schöneich's testimony on this issue—that *all* references to formulations with pH of 13 in the patent *except* the reference to a formulation with pH of 13 in the disputed claim are measured at standard temperature—was not credible. FOF ¶ 47. This is notable because Examples 3 and 4 are the only ones that provide for bulk solutions with a pH of 13 or higher. The claims only relate to bulk solutions with pH values of 13 or higher, making these examples highly probative. And Dr. Schöneich's concession that the pH measurements in Examples 3 and 4 were made at standard temperature is why a POSA would understand that the "pH of 13" as identified in the claim language would refer to the same pH of 13—one measured on a standardized scale at standard temperature. FOF ¶¶ 43–47.

131. Third, the claim term itself is silent as to the temperature at which the pH value ("13 or higher") should be measured. This is consistent with the rest of the patent and the prosecution history, which nowhere identifies a temperature for measuring bulk solution pH. FOF ¶¶ 25, 28. For that matter, the intrinsic record does not discuss or even suggest modifying pH by altering temperature; it only contemplates adjustment by addition of alkaline ingredients. Nor does the intrinsic record anywhere discuss, let alone define, the bulk solution's "actual" or "operating" temperature, either. The claim merely speaks of "form[ing]" a "lyophilized pharmaceutical composition" "from a bulk solution having a pH of

13 or higher." JTX-1.0010 (col. 18, ll. 51–52) (emphasis added); JTX-2.0011 (col. 19, ll. 51–52) (same). The claim does not specify a time or stage at which pH of the bulk solution should be measured.

132. However, a given manufacturer's processes may differ from another's, and the difference in processes may entail changes in temperature for the bulk solution. [redacted] FOF ¶ 64; PTX-7.0005. Without a standardized temperature to measure pH, a POSA would not and could not understand the claim language to identify any specific stage of the manufacturing process at which the pH must be measured. [redacted] FOF ¶¶ 59, 64. Only Mylan's position accounts for this reality. Actelion's position would lead to differing pH values for the same bulk solution at different stages of manufacture—a position that would render the claims indefinite, as discussed below.

133. "pH of 13" must refer to a standard-temperature benchmark to account for and avoid complications from variability in processes and conditions for the bulk solution, both between manufacturers and within manufacturers.

ii. Extrinsic Evidence supports a conclusion that "pH" in the context of the patents refers to pH as measured at standard temperature.

134. First, as noted, USP<791> prescribes that for pH, measurements be made at 25 ± 2°C unless a different temperature for measurement is specified in a USP monograph. FOF ¶ 22; DTX-6.0002. Dr. Hensler testified, based on his knowledge of the USP and the pharmaceutical industry, that a POSA in the field of pharmaceutical

manufacturing will understand USP in this way and therefore rely on industry standard techniques when testing the bulk solution for infringement. FOF¶¶ 54–55; *see also* ***Wellman***, 642 F.3d at 1367 ("The record suggests no reason that a person of skill in the art would have been incapable of applying those . . . standards to the claimed invention to achieve consistent, repeatable . . . measurements."). This testimony and USP are both consistent with the intrinsic evidence, which indicates pH values are to be understood at standard temperature. Dr. Schöneich's atextual reading of the claim is not credible; it would render the term "pH of 13" variable and unfixed, and result in a patent that uses inconsistent pH scales despite explicitly defining "alkaline" as "pH>7."

135. It was undisputed that a POSA would look to and rely upon USP for relevant manufacturing standards. FOF ¶ 22. The USP prescribes standard measurements, tests, and procedures that govern pharmaceutical manufacturing. FOF ¶ 20. POSAs in the field of pharmaceutical manufacturing rely upon and incorporate USP standards at every stage of the development and manufacturing process. FOF ¶ 22. A POSA would have read the patents-in-suit through the lens of the USP. FOF ¶¶ 24, 55. Dr. Hensler explained there was no reason a POSA would have been incapable of applying USP standards in reading the patents or manufacturing the ANDA products. FOF ¶ 55. Rather, a POSA would have applied those standards—including USP standards for measuring pH—to the manufacture of a bulk solution. FOF ¶ 55. Indeed, the specification includes two references to USP—when identifying a specific ingredient in Flolan's diluent ("Water for Injection, USP"), JTX-1.0002 (col. 2, ll. 59–62), and when defining the term "self-preservation" as "the ability to pass USP preservative effectiveness test." JTX-1.0003 (col. 4, ll. 31–34). FOF ¶ 55.

This further underscores that the POSA will be familiar with and understand that USP pharmaceutical standards will govern the terms and substance of the patent and its claims. Id.

136. Second, the evidence established that both Mylan and Actelion measure the pH level of a bulk solution at standard temperature during manufacturing regardless of the "operating" temperature. PTX-69.0043–45; PTX-177.0025; DTX-112.001; FOF ¶¶ 58–59. Evidence of an inventor or patentee's own practice is relevant to the meaning of the term. *See, e.g.*, ***Oyster Optics, LLC v. Ciena Corp.***, 2020 WL 13891311, at *11 (N.D. Cal. Aug. 10, 2020) (White, J.) ("The Court cannot ignore the patentee's own understanding of the claim terms . . . ."); ***ASM Am., Inc. v. Genus, Inc.***, 401 F.3d 1340, 1347 (Fed. Cir. 2005) (extrinsic evidence of plaintiff's and inventor's use of term relevant to POSA's understanding of claim term); ***Butamax(TM) Advanced Biofuels LLC v. Gevo, Inc.***, 746 F.3d 1302, 1313 (Fed. Cir. 2014) (considering "extrinsic evidence," such as "Butamax's internal documents," in considering meaning of claim term), *vacated on other grounds*, 574 U.S. 1133 (2015).

137. Dr. Schöneich testified that Actelion's process is an embodiment of the claims at issue. FOF ¶ 59. Actelion's practice of heating a sample to room temperature to test whether its pH is "13 or higher" and the direct reliance on USP <28> (which incorporates USP <791> for pH measurements) in its Analytical Procedures submitted to the FDA, FOF ¶ 58, is compelling extrinsic evidence that a POSA understands the claim language to refer to "pH of 13 or higher" on a standard temperature scale, not to signify "pH of 13 or higher" at whatever an unspecified "operating" temperature of the bulk solution happens to be.

Cf. ***Bristol-Myers***, 288 F.Supp.2d at 585–86 ("Testimony against a patentee's own interest . . . is perhaps the 'most persuasive extrinsic evidence.'" (quoting ***Evans Med. Ltd. v. American Cyanamid Co.***, 11 F.Supp.2d 338, 350 (S.D.N.Y. 1998), *aff'd*, 215 F.3d 1347 (Fed. Cir. 1999)). This is why the parties stipulated Veletri is an embodiment of the Asserted Claims—Veletri's bulk solution has a pH of 13 or higher [redacted] at room temperature. FOF ¶ 59. Mylan's bulk solution does not. Id.

iii. Alternative Factual Holding: Plain and Ordinary Meaning and Test for Infringement

138. The conclusion as to the temperature at which the bulk solution pH is measured would be the same even if the parties' dispute is understood not as a claim construction issue, but rather a purely factual dispute over the "plain and ordinary meaning" of "pH" in the context of this claim term and the patent as a whole, *see* ***Apple, Inc. v. Samsung Elecs. Co.***, 2014 WL 660857, at *3 (N.D. Cal. Feb. 20, 2014) (Koh, J.), or raising "factual questions relating to the test for infringement." ***Lazare Kaplan Int'l, Inc. v. Photoscribe Techs., Inc.***, 628 F.3d 1359, 1376 (Fed. Cir. 2010). "[T]he ordinary meaning of a claim term is its meaning to the ordinary artisan after reading the entire patent." ***Aylus Networks, Inc. v. Apple Inc.***, 856 F.3d 1353, 1358 (Fed. Cir. 2017) (quotation marks omitted); *see* ***Aventis Pharms. Inc. v. Amino Chemicals Ltd.***, 715 F.3d 1363, 1373 (Fed. Cir. 2013) ("The written description and other parts of the specification . . . may shed contextual light on the plain and ordinary meaning.").

139. The same intrinsic and extrinsic evidence discussed above supports the exact same conclusion if understood as a factual finding. Accordingly, even were this

Court to deem the claim construction issue "waived" as Actelion urges, the conclusion is the same: pH in the claims at issue denotes pH at standard temperature.

iv. Well-reasoned precedent supports either a construction or finding that pH values refer to standard temperatures.

140. Concluding that the claims refer to pH at standard temperature—whether as a legal or factual matter—accords with the reasoning of ***Dow Chem. Co. v. Halliburton Co.***, 631 F.Supp. 666, 688–89 (N.D. Miss. 1985), which observed:

> The pH number is an index to indicate the acidity or alkalinity of an aqueous solution. The pH is normally measured at room temperature, and a measurement not showing a temperature would connote measurement at room temperature to one skilled in the art. If the pH is 7, the solution is considered to be neutral; if the pH is above 7, it is alkaline or basic; and if the pH is below 7, it is acidic. The range of acidity and alkalinity extends from 0–14. . . . [O]ne skilled in chemical cleaning would know, even though there is no indication of the temperature of the pH measurement, that the pH measurement was done at essentially ambient temperatures, just as one skilled in the art would technically interpret the claims of the Lesinski patent as meaning pH measured at ambient temperature, which corresponds to pH measurements as practiced in the field.

141. The ***Dow Chemical*** court specifically rejected an "operating temperature" argument similar to the one Actelion urges:

> While it is true that the pH of the ammoniated EDTA is less than 8 at elevated operating temperatures, as numerically calculated, there is nothing

> misleading about the language of the patent. . . . The Lesinski patent in claim 6 defines the alkalinity of the ammoniated EDTA solution as being from 8 to 11. Examples 1 to 4 of the Lesinski patent connote to one skilled in the art that the measurement of pH was done at room temperatures, and not at the higher temperatures to which the solution was raised to speed up the rate of scale removal.

631 F.Supp. at 688. The same rationale applies here.

v. Literal Infringement: Conclusion

142. The parties' dispute concerns the "plain and ordinary meaning" of "pH of 13." As a matter of claim construction and/or fact-finding, the evidence—intrinsic and extrinsic—compels the conclusion a POSA understands "pH" to carry the plain and ordinary meaning in the pharmaceutical-manufacturing industry (*i.e.*, a value measured by default at a standard temperature), not an abstract concept as described in analytical textbooks (*e.g.*, a simple concentration of hydrogen ions). Actelion's position would improperly "replace a[] claim term" (pH) "with a different term" (ion concentration). ***Wellman***, 642 F.3d at 1367.

143. Because the claim at issue refers only to "pH of 13," it signifies a pH of 13 as measured at 25 ± 2°C. This conclusion is dispositive of literal infringement. In order for a claim to be literally infringed, an accused product must meet every limitation specified in the claim. *See, e.g.*, ***Becton Dickinson and Co. v. C.R Bard, Inc.***, 922 F.2d 792, 796 (Fed. Cir. 1990). When measured at 25 ± 2°C, it is undisputed that Mylan's ANDA product does not meet the "13 or higher" limitation, and therefore does not infringe. FOF ¶ 61.

[redacted] Id.[8] Accordingly, Mylan's product does not literally infringe claims 1, 6, 8, 10, 11, 16, 18, 20, and 22 of the '802 patent and claims 16, 18–22, and 24–42 of the '227 patent.

144. Actelion failed to carry its burden to prove infringement. Even if Actelion were correct that pH is measured at the "operating temperature" of the bulk solution (which it is not), Actelion failed to prove infringement by a preponderance of the evidence. Dr. Schöneich only tested a recreated bulk solution at 5°C. FOF ¶ 64. He did not test Mylan's bulk solution at its "actual" or "operating" temperatures prior to lyophilization. FOF ¶¶ 64–65. [redacted] FOF ¶¶ 64–66. In other words, Actelion presented no evidence of the pH of the bulk solution at the "operating temperature" when the claimed "lyophilized pharmaceutical composition" is in fact "formed from" it. FOF ¶ 70. This precludes a finding of infringement even if Actelion's construction of "pH of 13" were to be adopted.

D. Mylan does not infringe under the doctrine of equivalents.

145. To prove infringement under the doctrine of equivalents, the patentee must show that an accused product or process contains every element of the patented invention or its substantial equivalent. *See* ***Warner-Jenkinson Co., Inc. v. Hilton Davis Chemical***

[8] The label for Mylan's ANDA product is not to the conrtrary—it says nothing about the bulk solution, and Mylan is required by law to reproduce its contents in any event. *See* 21 C.F.R. § 314.94.

Co., 520 U.S. 17, 40 (1997). This is a doctrine of limited scope and applicability, "not simply the second prong of every infringement charge, regularly available to extend protection beyond the scope of the claims." ***Amgen Inc. v. Sandoz Inc.***, 923 F.3d 1023, 1029 (Fed. Cir. 2019), *modified on reh'g*, 776 Fed.App'x 707 (Fed. Cir. 2019). Here, Actelion has failed to meet its burden for multiple, independent reasons.

i. Disclosure Dedication

146. Actelion is precluded from proving infringement under the doctrine of equivalents by the doctrine of disclosure dedication. "[W]hen a patent drafter discloses but declines to claim subject matter, . . . this action dedicates that unclaimed subject matter to the public." ***Johnson & Johnston Assocs. Inc. v. R.E. Serv. Co.***, 285 F.3d 1046, 1054 (Fed. Cir. 2002). Such "unclaimed subject matter must have been identified by the patentee as an alternative to a claim limitation." ***Pfizer, Inc. v. Teva Pharms., USA, Inc.***, 429 F.3d 1364, 1379 (Fed. Cir. 2005). "[A] patentee cannot narrowly claim an invention to avoid prosecution scrutiny by the PTO, and then, after patent issuance, use the doctrine of equivalents to establish infringement because the specification discloses equivalents." ***Johnson & Johnson***, 285 F.3d at 1054.

147. Here, the patent claims a "bulk solution having a pH of 13 or higher." JTX-1.0010 (col. 18, ll. 51–52); JTX-2.0011 (col. 19, ll. 51–52). The specification, however, clearly identifies specific, alternative pH values—"Preferably, the base is added so that the pH of the bulk solution is greater than 11, preferably greater than 12, and, most preferably greater than 13." JTX-1.0004 (col. 5, ll. 35–38); JTX-2.0004 (col. 5, ll. 44–47). Actelion deliberately did not claim those values; instead, it narrowed the claim to "13 or

higher." It has therefore dedicated bulk solutions having a pH of between 11 and 12.98 as well as between 12 and 12.98 to the public. *See* ***Brunswick Corp. v. United States***, 152 F.3d 946, 1998 WL 163700, at *5 (Fed. Cir. 1998) (unpublished) (precluding doctrine of equivalents where "values disclosed [in specification] for at least two of the sheets indicate surface resistivities below the claimed range of 100 to 1000 ohms, but within the range of equivalents sought by Brunswick in this case"). [redacted] But even more to the point, the specification described yet another alternative: "[t]he pH of the bulk solution is preferably adjusted to about 12.5–13.5." JTX-1.0004 (col. 5, ll. 41–43); JTX-2.0004 (col. 5, ll. 50–52). There, a POSA can readily identify a pH range of the bulk solution from 12.5–12.98 [redacted] that was disclosed, but not claimed. FOF ¶ 74. Dr. Schöneich did not dispute these factual findings and did not consider the doctrine of disclosure dedication. FOF ¶ 75. Any one of these disclosed alternatives alone prevents Actelion from proving infringement of Mylan's ANDA product under the doctrine of equivalents as a matter of law.

ii. Prosecution History Estoppel

148. Separately, Actelion cannot prove infringement under the doctrine of equivalents because it is precluded from doing so by the separate and independent doctrine of prosecution history estoppel. "The prosecution history constitutes a public record of the patentee's representations concerning the scope and meaning of the claims, and competitors are entitled to rely on those representations when ascertaining the degree of lawful conduct, such as designing around the claimed invention."

Hockerson-Halberstadt, Inc. v. Avia Grp. Int'l, Inc., 222 F.3d 951, 957 (Fed. Cir. 2000). "Prosecution history estoppel" bars application of the doctrine of equivalents "[w]here the original application once embraced the purported equivalent but the patentee narrowed his claims to obtain the patent or to protect its validity." ***Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.***, 535 U.S. 722, 734 (2002). It "preclud[es] a patentee from regaining, through litigation, coverage of subject matter relinquished during prosecution of the application for the patent." ***Wang Lab'ys, Inc. v. Mitsubishi Elecs. Am., Inc.***, 103 F.3d 1571, 1577–78 (Fed. Cir. 1997). "A patentee who narrows a claim as a condition for obtaining a patent disavows his claim to the broader subject matter, whether the amendment was made to avoid the prior art or to comply with § 112." ***Festo***, 535 U.S. at 737.

149. Actelion only received a patent because the Examiner deemed a formulation at "pH of 13 or higher" to be a critical dividing line between (patentable) unexpected results and (unpatentable) results that were obvious from the prior art, chiefly Watts. FOF ¶ 50.

150. By repeatedly narrowing its claim to overcome the Examiner's objections, ultimately changing it from pH "greater than 12" to "pH of 13 or higher," FOF ¶ 49, Actelion surrendered any claim to products with a bulk solution greater than 12 but *lower* than 12.98, as measured at standard temperature. ***Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.***, 344 F.3d 1359, 1365 (Fed. Cir. 2003) (recognizing "presumption that a narrowing amendment made for a reason of patentability surrenders the entire territory between the original claim limitation and the amended claim limitation"). Mylan was "entitled to rely on [Actelion's] representations." ***Hockerson-Halberstadt***, 222 F.3d at 957.

Applying the doctrine of equivalents in this case would contravene the Federal Circuit's consistent position on permissible uses of that doctrine, dramatically expanding the scope of the claims and rendering their explicit, precise pH limitation effectively meaningless.

151. Actelion bears the burden of refuting the presumption of surrender. *See* ***Festo***, 344 F.3d at 1365. It failed to do so here as, once again, its expert provided no opinion whatsoever on the doctrine. FOF ¶¶ 80–81. Authorities concerning amendments "tangential" to the purported equivalent are inapposite. [redacted] The amendment narrowing the claim to pH of 13 or higher is *central* to the purported equivalent, not tangential: It was made specifically to avoid prior art that, according to the Examiner, would have encompassed the purported equivalent. [redacted] the Examiner rejected "greater than 12" and required a hard line at 13. Concluding that "pH of 13" refers to pH at standard temperature *necessarily* estops Actelion from proving infringement under the doctrine of equivalents.

152. Any argument that the amendment is "tangential" would necessarily assume that pH of 13 refers to a concentration of ions contingent on temperature, not fixed values of "pH" as measured at a standard temperature. But, as discussed above, the patent does not claim specific hydrogen ion concentrations; it claims a range of standardized pH values as readily understood by a POSA. Had Actelion intended to capture the purported equivalent, it would have drafted an amendment explicitly defining the alkalinity of the claimed bulk solution in terms of *ion concentrations*, not standard-temperature pH values.

Cf. ***Festo***, 535 U.S. at 741. It did not; it surrendered all standard-scale pH values below 12.98 to get its patent. Accordingly, it cannot prove infringement under the doctrine of equivalents as a matter of law.

iii. Failure of Proof

153. This Court returns to the fact that even if Actelion was not barred from proving infringement by disclosure dedication or prosecution history estoppel, it failed to carry its burden to prove [redacted] is "equivalent" to a pH of 13 or higher under the so-called "function-way-result" test. Dr. Schöneich only offered testimony on the function-way-result test; Actelion did not present any evidence to support application of any other test for equivalence, including the "insubstantial difference" test. FOF ¶ 83. As a general matter, "non-mechanical cases may not be well-suited to consideration under" the so-called function-way-result test, which "seems to be particularly true in the chemical arts." ***Mylan Institutional LLC v. Aurobindo Pharma Ltd.***, 857 F.3d 858, 867 (Fed. Cir. 2017).

154. With respect to ANDA litigation, bioequivalency alone does not and cannot establish infringement under the doctrine of equivalents; if it "meant per se infringement, no alternative to a patented medicine could ever be offered to the public during the life of a patent." ***Abbott Lab'ys v. Sandoz, Inc.***, 486 F.Supp.2d 767, 776 (N.D. Ill. 2007); *aff'd*, 566 F.3d 1282 (Fed. Cir. 2009). And that makes sense—a generic drug manufacturer is required by law to show its generic drug product is bioequivalent to, and has the same label as, the brand manufacturer's drug. *See, e.g.*, 21 C.F.R. § 314.94; FOF ¶ 84. That is why "the doctrine of equivalents must be applied to individual elements of the claim, *not to the invention as a whole*." ***Warner-Jenkinson***, 520 U.S. at 29 (emphasis added); *see*

Aurobindo, 857 F.3d at 867 ("The 'result' of using a claimed compound may be more easily evaluated, . . . [but] that is not how infringement under FWR is determined. It must be determined on a limitation-by-limitation basis."). Further, a plaintiff cannot rely on the doctrine of equivalents "if applying the doctrine would vitiate an entire claim limitation." ***Asyst Techs., Inc. v. Emtrak, Inc.***, 402 F.3d 1188, 1195 (Fed. Cir. 2005).

155. Actelion failed to carry its burden to prove infringement under the function-way-result test for equivalence because its arguments and evidence operated at an impermissibly high level of generality and would result in vitiation of the "pH of 13 or higher" limitation.

156. First, Dr. Schöneich testified that his analysis, Actelion's sole support for applying the doctrine of equivalents, did not relate to *limitations*. Instead, he admitted that he "perform[ed] a scientific analysis of the function, the way, and the result of *Mylan's bulk solution*," not the "pH of 13 or higher" limitation. FOF ¶ 85.

157. Second, in any event, Actelion's function-way-result analysis was defective because it collapsed the "function" of the pH element (modifying the ion concentration) with the "way" it does it. *See* ***Aurobindo***, 857 F.3d at 868. ("[T]hat is not considering the 'way' the oxidation works. Manganese dioxide and silver oxide may have the same function, but the question is whether they operate in the same way."). Adding sodium hydroxide is a "way" disclosed in the patent. It changes the relative *composition*, the ingredients, of the bulk solution. *E.g.*, JTX-1.0007 (col. 11, l. 63-col.12, l. 34). Adding a different, unclaimed alkaline substance (*i.e.* something other than sodium hydroxide) might therefore be equivalent. But adjusting temperature is not a "way" disclosed in the patent.

158. Dr. Schöneich's own testimony indicated that the "way" temperature affects pH is different from adding substances; it concerns modifying the *behavior of water*. FOF ¶ 85 (citing [Doc. 225 at 22:3–9, 37:7–14 ("At cooler temperatures, fewer molecules of water break up to get hydrogen ions. At higher temperature, more water molecules break up to create hydrogen ions.")]). Actelion may have identified a function (lowering hydrogen ion concentration) and result (increasing stability), but failed to adequately address, and thus to meet its burden, on the separate question of the *way*.

159. Actelion therefore failed to meet its evidentiary burden of proving infringement under the function-way-result theory of equivalence. Applying the doctrine here would vitiate the "pH of 13 or higher" claim limitation—a bright-line separation between pH values measured at standard temperature—because there is "a lack of equivalence based on the evidence presented and the theory of equivalence asserted." ***Cadence Pharms. Inc. v. Exela PharmSci Inc.***, 780 F.3d 1364, 1371 (Fed. Cir. 2015).

iv. Doctrine of Equivalents: Conclusion

160. Actelion is precluded from relying on the doctrine of equivalents to prove infringement of the claims at issue based on disclosure dedication and prosecution history estoppel. In any event, Actelion has failed to meet its burden to prove equivalence. Mylan therefore does not infringe claims 1, 6, 8, 10, 11, 16, 18, 20, and 22 of the '802 patent and claims 16, 18–22, and 24–42 of the '227 patent under the doctrine of equivalents.

E. Actelion's urged pH measurement would render the patent indefinite, and therefore, invalid.

161. Further supporting a conclusion that pH in the claims at issue refers to pH at standard temperature is that, were the Court to adopt (which it is not) Actelion's reading of pH, Actelion cannot prevail because the claim would be invalid as indefinite.

162. "[A] patent is invalid for indefiniteness if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention." ***Nautilus, Inc. v. Biosig Instruments, Inc.***, 572 U.S. 898, 901 (2014). "The claims, when read in light of the specification and prosecution history, must provide objective boundaries for those of skill in the art." ***Interval Licensing LLC v. AOL, Inc.***, 766 F.3d 1364, 1371 (Fed. Cir. 2014).

163. "[P]recedent [] hold[s] claims indefinite in particular circumstances where the claims require measured quantities (absolute or relative), different techniques for such measurements are known in the art and some produce infringing results and others not, the intrinsic evidence does not adequately specify the technique or techniques to use, and extrinsic evidence does not show that a relevant skilled artisan would know what technique or techniques to use." ***Forest Labs., Inc. et al. v. Teva Pharms. USA, Inc.***, 716 Fed.App'x 987, 994 (Fed. Cir. 2017).

164. If the claim specifies a *substance* (bulk solution) and *pH value* (13 or higher) but the patent leaves the temperature of measurement an open variable, it does not reasonably inform a POSA about the scope of what is claimed, and therefore would be invalid. This is true for several reasons. First, under Actelion's theory, different

manufacturers may use different standards of measurement. FOF ¶ 89. Without intrinsic guidance from the patent, one manufacturer may rely on USP, while another could follow Dr. Schöneich's approach and measure at "operating temperature." The differing approaches could lead to some measurements with infringing values and others with non-infringing values. Id.

165. This raises a second problem—what the "operating temperature" of the bulk solution actually is. The patents do not define this term. Dr. Schöneich did not provide any clear and readily comprehensible definition of the term for a POSA. FOF ¶ 90. As previously noted, the claim language does not specify *when* or at what *stage* the pH of the bulk solution should be assessed. It states only that a lyophilized composition is "formed from a bulk solution having a pH of 13 or higher." JTX-1.0010 (col. 18, ll. 51-52); JTX-2.0011 (col. 19, ll. 51-52). The specification likewise only indicates that the pH is adjusted *before lyophilization*. *See* JTX-1.0006 (col. 9, ll. 50-53); JTX-2.0006 (col. 9, ll. 50–53) ("[T]he pH of the solution containing epoprostenol and arginine was adjusted to 13.0 with sodium hydroxide, and lyophilized.").

166. Different manufacturers will have different processes and conditions as the bulk solutions are produced— [redacted] There are any number of conditions the bulk solution may be exposed to before lyophilization. [redacted] FOF ¶ 91. [redacted] FOF ¶ 91. If temperature is not standardized, a bulk solution [redacted]

[redacted] may have varying temperatures, engendering further uncertainty as to when measurements should be made in determining whether a product infringes or not. Standardization of the temperature of pH measurement remedies this concern—but if Actelion's non-standardized pH temperature position were adopted, the claims would fail to inform a POSA with reasonable certainty the scope of the purported invention. FOF ¶ 91.

167. Actelion's reading fails to specify the measurement, technique, or conditions for assessing whether a given bulk solution infringes. That, in turn, would not provide adequate guidance to a POSA. Under Actelion's reading, claims 1, 6, 8, 10, 11, 16, 18, 20, and 22 of the '802 patent and claims 16, 18–22, and 24–42 of the '227 patent would be invalid for indefiniteness.

III. CONCLUSION

168. Actelion failed to prove by a preponderance of the evidence that Mylan's ANDA product infringes the limitation of "a bulk solution having a pH of 13 or higher" because a POSA properly understands pH in the context of this patent to be measured at standard temperature, and it is undisputed that Mylan's ANDA product does not infringe when measured at standard temperature. Actelion fails to prove infringement under the doctrine of equivalents because it is barred from doing so by the doctrines of disclosure dedication and prosecution history estoppel, and because it did not meet its burden of proving equivalence on its chosen theory.

169. Mylan does not infringe under this Court's claim construction since the bulk solution will never have a pH of 12.98 or higher.

It is so **ORDERED**.

The Clerk is directed to transmit copies of this Order to any counsel of record herein.

DATED: March 7, 2024.

JOHN PRESTON BAILEY
UNITED STATES DISTRICT JUDGE